ANNALS of ALLERGY

Published by
The American College of Allergists

Volume 19 August, 1961 Number 8

FREE AMINO ACID CONTENT OF POLLEN

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ALTHOUGH THE CHEMISTRY of the hay fever producing substances present in pollens has been studied for over fifty years, the exact make-up of the substance or group of substances which bring about the allergic manifestations attributed to pollen has not yet been determined.

Early investigators indicated that the active principle in pollen was protein. However, Grove and Coca[1] found in 1923 that all of the nitrogen of a pollen extract could be removed by dialysis, and the extract would retain its atopic activity. Since that time, the active materials in pollen have been frequently referred to as protein-like materials which may also contain some carbohydrates.

Caulfield and co-workers[2] in their investigation also isolated an active material rich in carbohydrate. The protein was separated from the carbohydrates by means of precipitation. The final product contained 1.5 per cent nitrogen and, after hydrolysis, yielded 58 per cent reducing sugar. This fraction was active by both direct skin test and passive transfer. These investigators believed that protein could not have been present, because this carbohydrate fraction failed to produce anaphylactic shock in guinea pigs that had been previously sensitized to the whole pollen extract.

Newell[3] in his review of the chemical studies of the allergens in pollen, stated that the characteristic allergenic properties are probably attributed to several substances that are of a complex nature. These allergens are

This project was conducted as a part of the Internal Research Program of Southwest Research Institute.

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Presented at the Seventeenth Annual Congress of The American College of Allergists, March 15, 1961 in Dallas, Texas.

smaller in molecular size than the proteins, which range in size from a molecular weight of 6000 to several million, and have a molecular weight of 5000 or less. It appears that most allergens are much lower in molecular weight.

In reviewing the various investigations on the composition of allergens, it appears that Newell's[3] conclusions are still valid. He stated that the sum of all of the work done is difficult to evaluate because of contradictory reports and lack of uniform methods for quantitative studies. Richter and Sehon[4] appear to confirm Newell's conclusions. In their summary, they state that none of the investigators have provided satisfactory proof that the allergens have been separated in pure form. Goldfarb, *et al*,[5] however, did isolate a fraction from giant ragweed pollen that appeared to be a single entity known as Trifidin A. When dissolved in distilled water and kept in a cold room, however, it degraded into three components—a ninhydrin-stainable material, arabinose, and some simple sugars.

Sehon and Richter[6] separated a fraction from short ragweed pollen which was shown to contain a pigment and peptide(s). This fraction was composed of eight amino acids: arginine, lysine, glutamic acid, glycine, alanine, hydroxyproline, valine and norleucine. The pigment could be removed from this fraction without loss of allergenic activity. However, hydrolysis of the peptide(s) resulted in a complete loss of allergenic activity. From their work, it would appear that a substance similar to a peptide is the allergen. Further, they have shown that a very dilute fraction was allergenically as potent as whole water soluble extract of ragweed pollen. Since this fraction, along with other highly allergenically active fractions, contains some nitrogen material, it was suggested that the allergenicity of ragweed pollen is due to peptide(s) which may be complicated with other materials such as proteins, carbohydrates or pigments.

METHODS

The majority of pollens used in this investigation were collected by the senior investigator (locally) or by pollen collectors specifically for this investigation. The pollens were separated by mechanical means and were not chemically treated in the separation process.

Aqueous pollen extracts were prepared containing one gram of pollen per ten milliliters of extract. They were kept overnight at 4° C during the extraction process. The amino acids in the water extracts were then separated by paper chromatography.

Samples of 100 microliters each were run in triplicate. In some cases, the sample size was altered in order to facilitate the quantitative analysis. Two dimensional chromatograms were run on Whatman No. 1 paper. The solvents used were composed of butanol, acetic acid and water (4:1:1), and a 70 per cent 2-4 lutedine as the second solvent. The chromatograms were developed in 0.25 per cent ninhydrin (1, 2, 3-Triketohydrindene) in

acetone. The spots were identified by comparison with chromatograms of known amino acids. Chart 1 shows a typical chromatogram of amaranth pollen.

Histidine, arginine, lysine and glutamic acid were separated by paper electrophoresis. A Gordon-Micro Multiple Cell Paper-Electrophoresis ap-

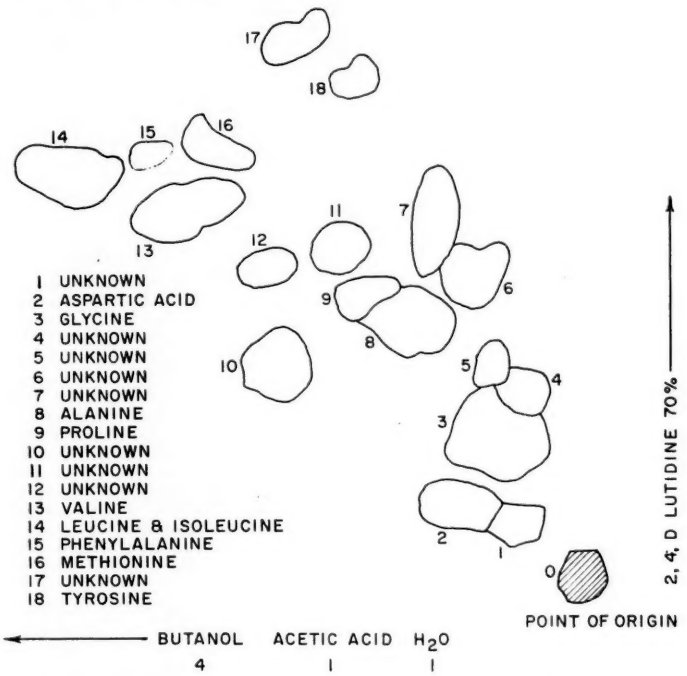

Chart 1. Chromatogram of amaranth pollen, *Ameranthus palmeri.*

paratus purchased from Microchemical Specialties Co., Berkeley, California, was used. The electrophoretic separation was conducted in a 0.25 molar acetic acid, having a pH of 2.7 at 250 volts. Five samples were run simultaneously on individual paper strips.

Quantitative analyses on the amino acids were performed according to the method described by Block, *et al,*[7] using stannous chloride, methyl cellosolve and ninhydrin. The various spots were removed from the chromatogram and the amino acids were eluted from the paper. Standards, blanks and reagent blanks were included in each analysis. Optical densities were determined on a Spectronic 20 spectrophotometer. Quantitatively, the amino acids are recorded as micromoles of amino acids per gram of pollen (Table I). Although a total of 107 different pollens (Table II) were investigated for the presence of amino acids, quantitative determinations were made of only twenty-one. Solvents used for separating the amino

TABLE I. MICROMOLES AMINO ACID PER GRAM OF POLLEN

Amino Acid	Pines		
	Halepense	Longleaf	Shortleaf
Isoleucine } Leucine	6.7	32.1	13.5
Phenylalanine	+*	2.2	0.7
Proline } Hydroxyproline	16.9	5.8	1.0
Alanine	8.9	44.9	18.0
Glycine	5.2	17.7	8.7
Aspartic	13.5	10.4	10.7
Methionine	+	1.6	0.4
Valine	5.3	19.1	11.5
Tyrosine	+	1.8	1.4
Arginine	10.2	35.1	1.7
Lysine	11.9	+	3.6
Histidine	3.9	−	−
Glutamic	+	−	2.7

*+ Trace
**− Not detected

Amino Acid	Grasses			
	Rye	Timothy	Bermuda	Johnson
Isoleucine } Leucine	65.6	6.4	34.9	13.1
Phenylalanine	14.7	−**	3.7	0.03
Proline } Hydroxyproline	8.3	1.0	32.3	7.1
Alanine	98.9	16.0	30.0	24.2
Glycine	22.9	15.5	20.1	37.3
Aspartic	12.9	+	17.7	1.9
Methionine	14.5	+	+	+
Valine	44.4	8.5	20.3	7.7
Tyrosine	9.8	0.2	2.6	1.3
Arginine	33.0	+	36.5	+
Lysine	11.3	−	17.3	−
Histidine	−	−	7.3	+
Glutamic	−	+	25.4	−

*+ Trace
**− Not detected

Amino Acid	Trees		
	American Elm	Cedar Elm	Hackberry
Isoleucine } Leucine	27.6	9.7	40.0
Phenylalanine	1.0	3.9	1.7
Proline } Hydroxyproline	25.0	20.2	36.1
Alanine	43.1	16.0	42.7
Glycine	22.4	14.0	26.9
Aspartic	3.6	19.5	8.4
Methionine	1.2	4.4	1.2
Valine	17.7	7.7	36.9
Tyrosine	0.9	1.2	4.3
Arginine	7.0	−	−
Lysine	29.5	5.1	29.5
Histidine	−	−	−
Glutamic	−	5.9	21.

*+ Trace
**− Not detected

acids recorded in Table II were: butyl cellosolve and water (7:3); and isopropyl alcohol, acetic acid and water (7:2:1).

RESULTS

The data obtained from the quantitative analyses of the pollen extracts indicate the presence of essentially the same amino acids in all of the

TABLE I. MICROMOLES AMINO ACID PER GRAM OF POLLEN (CONTINUED)

Amino Acid	Common Weeds				
	Dock	Lambs-quarter	Burning Bush	Careless Weed	English Plantain
Isoleucine, Leucine	1.5	3.0	3.6	3.3	+
Phenylalanine	–	+	2.6	1.7	–
Proline, Hydroxyproline	+	6.7	2.1	+	+
Alanine	5.6	14.0	12.6	21.2	+
Glycine	1.7	10.4	26.8	2.3	4.1
Aspartic	–	4.6	2.9	3.6	+
Methionine	–	+	4.0	+	–
Valine	1.6	4.9	3.8	2.1	+
Tyrosine	+	+	2.6	+	–
Arginine	6.5	9.5	12.3	+	1.5
Lysine	10.1	–	+	–	10.0
Histidine	+	–	+	–	–
Glutamic	8.5	21.1	9.5	4.1	+

*+ Trace
**– Not detected

Amino Acid	Ragweed Family					
	Short	Giant	Western	Common Sage	Mugwort	Goldenrod
Isoleucine, Leucine	7.1	4.8	10.8	43.0	35.0	3.1
Phenylalanine	+	–	+	0.8	2.4	0.7
Proline, Hydroxyproline	+	5.9	3.5	9.0	5.6	2.5
Alanine	13.1	16.0	7.2	36.9	31.2	4.8
Glycine	5.7	5.7	9.2	22.9	17.9	0.9
Aspartic	+	+	+	+	4.2	3.2
Methionine	+	+	+	+	0.3	–
Valine	3.5	2.6	10.0	27.5	19.3	2.9
Tyrosine	+	+	+	+	1.9	+
Arginine	10.7	19.1	12.1	23.9	24.7	1.5
Lysine	–	–	–	10.8	24.7	+
Histidine	20.0	18.4	5.5	0.6	20.1	–
Glutamic	–	–	–	+	–	–

*+ Trace
**– Not detected

pollens that were analyzed (Table I). While essentially the same amino acids were found in the various pollens, the quantity of the various individual amino acids varies considerably among the species as well as the plant families. Certain amino acids appear much more prominent in some plants than in others. This similarity was particularly outstanding in some of the tree pollens, such as elm and hackberry.

These findings are contrary to those of other investigators, as well as some of the early work in our own laboratory at the Southwest Research Institute, in which a lesser number of amino acids were reported.

It can be seen that there are indications of a plant relationship between plant taxonomy and the amino acid content of the extracts: certain taxonomic groups have a high range of values and others, a low range. This striking similarity could be more readily observed immediately following the development of the chromatogram sheets before the colors began to fade.

The data further indicate that there is a direct relationship in the amino

TABLE II. NUMBER OF AMINO ACIDS OBSERVED IN PLANT POLLENS

Plant	Number of Amino Acids
GYMNOSPERMS	
TAXACEA	
Yew—*Taxus yew*	10
PINACEAE (PINES)	
White pine—*Pinus strobus*	6
Short leaf—*Pinus echinata*	4
Smooth pine—*Pinus halepense*	10
Hemlock spp.—*Tsuga spp.*	8
TAXODIACEAE (CYPRESS)	
Cypress—*Taxodium distichum*	10
CUPRESSACEAE (JUNIPERACEAE)	
Eastern red cedar—*Juniperus virginiana*	5
Mountain cedar—*Juniperus sabinoides*	6
Arbor vitae—*Thuja orientalis*	6
ANGIOSPERMS	
TYPHACEAE	
Common cattail—*Typha latifolia*	10
GRAMINEAE (GRASSES)	
Tribe 1: Festuceae	
Brome grass—*Bromus*	7
Red fescue—*Festuca rubra*	8
Meadow fescue—*Festuca elatior*	8
Bristle grass—*Setaria macrostachya*	8
Annual blue grass—*Poa annua*	8
Canadian blue grass—*Poa compressa*	8
Kentucky blue or June grass—*Poa pratensis*	5
Saltgrass—*Distichlis spicata*	6
Orchard grass—*Dactylis glomerata*	8
Tribe 2: Hordeae	
Quackgrass—*Agropyron repens*	7
Perennial rye grass—*Lolium perenne*	7
Italian rye grass—*Lolium multiflorum*	9
Italian rye grass—*Lolium italicum*	9
Tribe 3: Aveneae	
Tall oats grass—*Arrhenatherum elatius*	7
Tribe 4: Agrostideae	
Timothy—*Phleum pratense*	7
Red top—*Agrostis alba*	4
Tribe 5: Chlorideae	
Bermuda grass—*Cynodon dactylon*	12
Buffalo grass—*Buchloe dactyloides*	10
Tribe 6: Phalarideae	
Tribe 7: Zizaneae	
Tribe 8: Paniceae	
Tribe 9: Andropogoneae	
Johnson grass—*Sorghum halepense*	11
Sudan grass—*Sorghum sudanensis*	7
Tribe 10: Tripsaceae	
Maize or Indiana corn—*Zea mays*	6
LILACEAE	
Easter lily—*Lilium candidium*	7
CANNACEAE	
Canna sp.	8
SALICACEAE	
Black willow—*Salix nigra*	12
Cottonwood—*Populus deltoides*	9
Western cottonwood—*Populus sargentii*	19
White cottonwood—*Populus alba*	13
American aspen—*Populus tremuloides*	14
BETULACEAE	
White birch—*Betula alba*	10
Black birch—*Betula nigra*	10
Alder—*Alnus sp.*	11
Ironwood—*Ostrya virginiana*	8
American hazelnut—*Corylus americana*	7
FAGACEAE	
American beech—*Fagus grandifolia*	11
Live oak—*Quercus virginiana*	12
Black oak—*Quercus marilandica*	11
Bur oak—*Quercus marcrocarpa*	11
Red oak—*Quercus rubra*	11
Chestnut oak—*Quercus muhlenbergii*	11
JUGLANDACEAE	
California black walnut—*Juglans californica*	10
Scrub or river walnut—*Juglans rupestris*	9
Black walnut—*Juglans nigra*	10
Shellbark hickory—*Hicoria ovata*	10
Pecan—*Hicoria pecan (C. pecan)*	13

TABLE II. (CONTINUED)

Plant	Number of Amino Acids
ANGIOSPERMS *(continued)*	
ULMACEAE	
American elm—*Ulmus americana*	10
Red or slippery elm—*Ulmus fulva*	9
Fall blooming elm—*Ulmus crassifolia*	11
Chinese elm—*Ulmus pumila*	10
Hackberry—*Celtis occidentalis*	11
MORACEAE	
Red mulberry—*Morus rubra*	9
PLATANACEAE	
Sycamore—*Platanus occidentalis*	11
ROSACEAE	
Rosa sp.	6
MIMOSACEAE	
Mimosa—*Acacia spp.*	8
Huisache—*Acacia farnesiana*	10
Mesquite—*Prosopis juliflora*	11
ACERACEAE	
Box elder—*Acer negundo*	8
Maple—*Acer spp.*	8
EUPHORBIACEAE	
Chinese tallow—*Sapium sebiferma (Stillingia)*	4
Castor bean—*Ricinus communis*	10
OLEACEAE	
Ligustrum—*Ligustrum vulgare*	7
White ash—*Fraxinus americana*	14
Arizona ash—*Fraxinus velutina*	13
Red ash—*Fraxinus pennsylvanica*	13
ANACARDIACEA	
Smoke tree—*Pistacia texana*	11
POLYGONACEAE (BUCKWHEAT FAMILY)	
Curly or yellow dock—*Rumex crispus*	6
Sheep sorrel—*Rumex acetosella*	10
PLANTAGINACEAE	
English plantain—*Plantago lanceolata*	6
AMARANTHACEAE (PIGWEEDS, ET CETRA)	
Green amaranth—*Amaranthus hybridus*	10
Red root pigweed—*Amaranthus retroflexus*	12
Careless weed—*Amaranthus palmeri*	11
Spiny amaranth—*Amaranthus spinosus*	9
Western water hemp—*Acnida tamariscina*	9
CHENOPODIACEAE (CHENOPODS OR GOOSEFOOTS)	
Mexican firebush—*Kochia scoparia*	8
Shad. scale—*Atriplex confertifolia*	9
Wingscale—*Atriplex canescens*	7
Lambsquarter—*Chenopodium album*	7
Lambsquarter—*Chenopodium paganum*	11
Mexican tea—*Chenopodium ambrosioides*	10
Russian thistle—*Salsola pestifer*	10
COMPOSITAE	
ASTEREAE	
Goldenrod—*Solidago speciosa*	7
HELIANTHEAE	
Sunflower—*Helianthus annuus*	6
AMBROSIEAE (RAGWEEDS AND MARSH ELDERS)	
Rough marsh elder—*Iva ciliata*	11
Burweed marsh elder—*Iva xanthifolia*	10
Narrow leaf marsh elder—*Iva angustifolia*	10
Short ragweed—*Ambrosia artemisiifolia*	7
Giant ragweed—*Ambrosia aptera*	7
Western ragweed—*Ambrosia psilostachya*	8
Common franseria—*Franseria tenuifolia*	11
Desert franseria—*Franseria dumosa*	7
Canyon franseria—*Franseria ambrosioides*	7
XANTHIUM (COCKLEBURS)	
Cocklebur—*Xanthium speciosum*	11
Cocklebur—*Xanthium commune*	12
Cocklebur—*Xanthium spinosum*	11
ARTEMISIA (SAGEBRUSH, ET CETRA)	
Common sagebrush—*Artemisia tridentata*	8
Sand sagebrush (or silvery wormwood)—*Artemisia filifolia*	5
Common mugwort—*Artemisia vulgaris*	6
Annual wormwood (or annual sage)—*Artemisia annua*	7

acid content of pollens and their allergic potential. Those pollens with a high amino acid content also appear to be notable offenders in the causing of allergy.

The one notable exception is the Mountain Cedar *Juniperus sabinoides* (not included in the quantitative analyses) which is low in all of the amino acids, according to our findings. In the case of the Mountain Cedar, it is possible to conjecture that the relative abundance of the pollen is more significant than the quantitative chemical composition.

These data do not in any way indicate that the amino acids in themselves are the offenders, but the amino acids could be the constituents that make up a more complex substance which in turn is the offender.

It will be further noted that some of the pollens are relatively high, in certain amino acids but low in others. In addition, the chart indicates that some of the amino acids were too low in quantity to be measured on a Bausch and Lomb Spectronic 20 colorimeter, although they did appear as relatively prominent spots on the chromatogram.

DISCUSSION

The variation in results obtained in the number of amino acids observed can probably be attributed to several factors, including the solvents used, the temperature at which the separations are made, and the paper used. The age and maturity of the pollen, its water content and the plants from which the pollen was collected may be additional factors. In observing the pollination of Mountain Cedar *Juniperus sabinoides,* the senior investigator has noted that there is a difference of as much as three weeks in the time that pollen may be released from individual trees. Although the trees may be only a few hundred yards apart, for example, the pollen-release date between two trees may vary as much as three weeks. Certain trees have been observed regularly for over ten years, and, if weather conditions are normal, it is possible to predict the exact date on which trees will begin to pollinate.

There is a prevalent belief that all of the amino acids are essential to a living protoplasm; however, some plants do not fully mature the pollen and may consequently set seed without fertilization. Such pollen could be different from fully matured pollen. This phenomenon is particularly prevalent in the grasses, and is known as apomixis. The Cedar Elm *Ulmus crassifolia* has also been observed to set seed before the pollen has been released. All of these factors along with others may well be responsible for the variation in amino acid number and content of pollen observed. While a total of 107 (Table II) different pollens were investigated for amino acid content, quantitative analysis was made on only twenty-one (Table I). This number was sufficient to indicate the trend of amino acids in pollen quantitatively.

It will be further noted in Table II that there is a great variation in the number of amino acids recorded. The lowest numbers were observed in

Short Leaf Pine *Pinus echinata,* Red Top *Argrostis alba,* and Chinese Tallow *Sapium sebiferum* (stillingia). Some additional samples of Short Leaf Pine indicated the presence of a higher number which was large enough in quantity to permit separation. Again it should be pointed out that the number of amino acids recorded in Table II is probably not the total number in a pollen, but rather is an indicator of the quantity present in amounts large enough to be observed on the chromatogram. It is probable that some of the spots observed and recorded in Table II included one or more amino acids due to incomplete separation. Those having a higher number were also the ones with a higher total quantity. Those having a lower number had a lesser quantity with a large number present in such small quantity that the samples were too small to appear on the chromatograms. If larger samples were extracted, additional amino acids would probably appear as definite spots on the chromatograms. If this assumption is correct, then it may still be valid to predict that those pollens with a high amino acid content are also the most common offenders. Finally, this investigation is primarily of a fundamental nature, and not an attempt to solve the problem of the true cause of the allergic manifestation itself. The correlation of these data, however, along with additional chemical and clinical investigations, will bring us closer to the solution of this problem.

SUMMARY AND CONCLUSIONS

A total of 107 plant pollens were investigated for their amino acid content. Paper chromatographic procedures were used for separating the various amino acids. Quantitative analysis of twenty-one of the pollens was also made.

The plant pollens investigated included representatives of the various plant groups, such as the pines, junipers, cattails, grasses, dicotyledonous trees and shrubs, and common weeds (such as the amaranths, chenopods and plantain and the various members of the compositae or ragweeds). The number of amino acids observed in the various plants was higher than reported by previous investigators.

From this investigation, it appears that the plant pollens contain most of the amino acids. However, there is a wide variation in the quantity of the different amino acids found in different plant groups.

Although the total recorded count varied from four in Red Top to nineteen in one Poplar species, it is likely that those plants with a lower recorded number should actually be much higher. The number represents the spots that could be readily counted, and, because of incomplete separation, some of the spots probably represent one or more amino acids.

The recorded number may not represent the exact number of amino acids, but it is an accurate reflection of the quantity of amino acids within a particular species. Those with a lower number contain amino acids that are not readily separated, as well as small quantities of others which were

difficult to detect on the chromatograms. When the pollens were collected, it was observed that, in general, bees visit those plants with a larger number more frequently than those having a lower recorded number.

There appears to be some further correlation between amino acid content and those plants which are the most serious offenders in bringing about the allergic manifestation. The one notable exception is the Mountain Cedar *Juniperus sabinoides.* This correlation does not in any way indicate that the amino acids are the cause of hay fever. However, they probably are a part of a complex molecule which is the offender.

REFERENCES

1. Grove, E. F., and Coca, A. F.: The nature of the pollen atopen. Proc Soc Exper Biol, 21:48, 1923.
2. Caulfield, A. H. W., Brown M. H., and Waters, E. T.: Experiments to determine whether allergenically active substance in ragweed pollen extract is a single entity or multiple. J Allergy, 7:1, 1935-36.
3. Newell, G. M.: A review of chemical studies on the allergens in pollen. J Allergy, 13:177, 1942.
4. Richter, M. and Sehon, A. H.: Allergen of ragweed pollen. J Allergy, 31:111, 1960.
5. Goldfarb, A. R., Bhattacharya, A. K., and Koerner, S. K.: Preparation and immunologic properties of trifiden A an antigen from giant ragweed. J Immunol, 81:302, 1958.
6. Sehon, A. H., and Richter, M.: Studies on ragweed pollen. IV isolation and characterization of an allergenic fraction from ragweed pollen. J Immunol, 82:190, 1959.
7. Block, Richard J., Durrum, Emmett L., and Zweig, Gunter: A Manual of Paper Chromatography and Paper Electrophoresis. 3rd Ed. New York: Academic Press, Inc. 1955.

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FALLACIES

And so you think, do you, that the chief use of Logic, in real life, is to induce Conclusions from workable Premisses, and to satisfy yourself that the Conclusions, deduced by other people, are correct? I only wish it were! Society would be much less liable to panics and other delusions, and political life, especially, would be a totally different thing, if even a majority of the arguments, that are scattered broadcast over the world, were correct! But it is all the other way, I fear. For one workable Pair of Premisses (I mean a Pair that lead to a logical Conclusion) that you meet with in reading your newspaper or magazine, you will probably find five that lead to no Conclusion at all: and, even when the Premisses are workable, for one instance, where the writer draws a correct Conclusion, there are probably ten where he draws an incorrect one.—LEWIS CARROLL, "The Game of Logic," *(Mathematical Recreations of Lewis Carroll, 1:33).*

BACTERIAL ANTIGEN COMPLEXES (HOFFMANN)

An Evaluation of Skin Test Specificity Versus Patient Reaction

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IN chronic lung disease, and especially of those patients who have been diagnosed as having infectious asthma, chronic bronchitis, and pulmonary emphysema, some form of treatment other than symptomatic is indicated. No form of treatment, of course, could be expected to change the irreversible pathological findings which have developed, but anything which will offer the patients more than a gradual decline is worth considering. Antibiotic agents, at best, will only temporarily get rid of the infection which recurs amazingly soon after their administration is discontinued. If maintenance doses are given, apparently the organisms become fast within a short time. It seemed reasonable to us that if the natural immune response could be strengthened and the neutralization of sensitizing antibodies stimulated with suitable bacterial antigens, then better results in the treatment of these breathless patients might be achieved.

Many allergists have frequently wondered which vaccines to use and how to choose those most likely to benefit each individual case.[1,2,10,12] Commercial vaccines have been employed such as staphylococcus toxoid (Lederle); H. influenzae Serobacterin (Sharp & Dohme); Catarrhalis Immunogen (Parke, Davis); M.V.R.I. Bacterial Vaccine (Cutter), as well as autogenous and stock bacterial vaccines. The choice of which of these to use was made by skin testing the patient with a measured quantity of each. The vaccine which gave the largest immediate and/or delayed reaction was the one selected. If the patient did well on this type of treatment, it was continued; if he did not improve, another vaccine would probably have been tried. The lack of patient response to the vaccine which gave the largest positive skin reaction was so frequently observed that it inspired the present investigators to find not only a better tool, but also a better means of assessing the possibility of success before starting treatment.

Prompted by the encouraging results in children reported by several

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Presented at the Seventeenth Annual Congress of The American College of Allergists, Dallas, Texas, March 15, 1961.

authors[4,8,9] who used acellular bacterial antigen complexes (B.A.C.®)* in the treatment of recurrent respiratory infections and infectious asthma, we commenced our investigation in the latter part of 1955, using this material.

This report deals with 311 patients ill with chronic lung disease and pulmonary emphysema. Diagnoses were of asthma, chronic bronchitis, chronic sinusitis, or chronic rhinitis, although some patients had two or more of these conditions.

MATERIALS

Bacterial antigen complexes, in contrast to vaccines, are acellular and crystal clear. Ninety to ninety-five per cent of the non-essential sensitizing bulk of the vaccine has been eliminated, and up to 94 per cent of the sensitizing nitrogenous substances such as meat extracts, peptones, et cetera, present in the filtrate, have been removed.

The process used retains the essential protective substances of the bacterial cells such as polysaccharides in pneumococci, the "M" substance in hemolytic streptococci, and the Boivin antigens in Gram-negative bacteria. These substances are combined by the process of co-precipitation with the antigenic substances present in the filtrate. Such antigenic substances are scarlet fever toxin, hemolysins, leucocidins, fibrinolysins, dermonecrotic toxin, coagulase and hyaluronidase.

Bacterial antigen complex preparations apparently combine all antigens necessary for antibacterial and antitoxic immunity. Thus, they offer in one preparation, as, for instance, staphylococcal bacterial antigen complex, the antigenic equivalent of cellular vaccines prepared from staphylococci and the antigens in staphylococcus toxoids. The method used prevents denaturization, deterioration and subsequent loss of valuable antigenic properties which may occur in the production of vaccines by repeated washings and the use of heat or chemicals. These complexes are produced in several different bacterial combinations, standardized to a concentration of 120 micrograms of total nitrogen per milliliter and to a pH of 7.0.

The following bacterial antigen complexes were used in this investigation: The original series of 1, 2, 3, 4, 7, and 8 (Table I), which later were combined, in part, to make Pooled Stock No. 1 and No. 2 as follows: Pooled Stock BAC No. 1 was prepared from sixteen of those prevalent single strains in BAC 1-8, and another strain of *Streptococcus hemolyticus*, Group A, Granger (arthritic strain).

Pooled Stock BAC No. 2 was prepared from the seven strains of the series not used in BAC No. 1 with the addition of Gram-negative organisms (Table II).

As they became available, Respiratory BAC, Pooled Gram-negative BAC, and Special Hospital Staphylococcus BAC were added to our testing group. Each of these was used as a separate test in our routine workup.

*Manufactured by Hoffmann Laboratories, 666 Broadway, Paterson 4, New Jersey.

TABLE I. ORIGINAL BACTERIAL ANTIGEN COMPLEXES

Beta hemolytic streprococci, group A	No. 1. Griffith types 10, 14 and 19 No. 2. Griffith types 3, 12 and 18
Pneumococci (most prevalent in adults)	No. 3. Diplococcus pneumonia types I, II, III No. 4. Diplococcus pneumonia types V and VII and K. pneumoniae A. (B. Friedlander)
Pneumococci (most prevalent in children)	No. 5. Diplococcus pneumoniae types I, VI, XIV No. 6. Diplococcus pneumoniae types V, VII, XIX
Streptococcus viridans	No. 7. Strains 1551, 1822 and R 353
Various organisms	No. 8. Staphylococcus aureus and albus Neisseria catarrhalis Hemophilus influenzae A and B E. coli

METHOD

Each test dose of BAC was administered bi-weekly. A 27-gauge, ¼ inch, short-beveled needle attached to a ¼ ml tuberculin syringe was used to give 0.02 ml intradermally in the upper arm. An immediate skin reaction of wheal and erythema was measured and recorded twenty minutes later. Another reading and measurement for delayed skin reaction was done after twenty-four hours.

Every patient was seen daily and carefully interrogated to determine any difference in symptoms, particularly shortness of breath, wheezing, tightness of chest, cough or amount of sputum produced. Any change or lack of it was recorded by grading each symptom as mild, moderate or severe. No alteration in medication was made during the testing period except where absolutely necessary due to acute illness. In this case, testing was discontinued until the patient had fully recovered and was then resumed. Where any question arose as to the response to an individual BAC test, that particular one was repeated after completion of the series. Finally, over-all evaluation was undertaken.

TABLE II. BACTERIAL ANTIGEN COMPLEXES NOW IN USE

Pooled stock BAC No. 1.	Pneumococci types I, II, V, VII, and XIV H. streptococci, group A, types 3, 10, and 12 and Granger strain Strep. viridans strains R 1551, R 1822, and R 353 Staphylococci—albus and aureus N. catarrhalis E. coli H. influenzae A and B
Pooled stock BAC No. 2.	Pneumococci types III, VI and XIX and Klebsiellae pneumonia A (B. Friedlander) H. streptococci, group A, types 14, 18 and 19 Gram-negative organisms: B. pyocyaneus (pseudomonas aeruginosa), E. coli and B. lactis aerugenes
Gram-negative BAC	B. Pyocyaneus (pseudomonas aeruginosa), E. coli and B. lactis aerugenes*
Respiratory BAC	H. streptococci, group A: hemolytic, non-hemolytic and viridans; pneumococci; neisseria catarrhalis; coliform; H. influenzae; and staphylococcus aureus and albus
Staphylococci	Phage types 42B/52/80/81 or so-called "Hospital Staph."

*All are present in Pooled Stock No. 2

SKIN TESTS RESULTS

Figs. 1-5. Immediate skin reactions to Pooled No. 1, Pooled No. 2, Gram-negative, Respiratory and Hospital Staphylococcal BACs.

Figs. 6-10. Same patient. Delayed reactions seen twenty-four hours later of the same BAC injections.

Figs. 11-15. Immediate reactions obtained with the same BACs in a Negro patient's skin. Delayed reactions are not shown, because the reading must be made on the basis of induration rather than red-ness which is not visible.

The patient whose skin tests are illustrated in Figures 1-10 had an amelioration of symptoms with Pooled No. 2, Gram-negative and Hospital Staphylococcal BACs, while the patient whose skin tests are illustrated in Figures 11-15 responded only to Gram negative BAC. It may be added that some patients gave larger immediate and delayed skin reactions than those of the two patients illustrated here, but there was no change in symptoms with any of the tests.

When one or more of these complexes had produced any reaction in the patient, either for better or worse, that one was repeated. If the result could be duplicated, that particular BAC was chosen for treatment. When there had been noted definite improvement after the test dose in the symptoms cited above, the patient was continued on this same dose of BAC undiluted. If the injection produced a definite exacerbation of symptoms, then this particular BAC was diluted 1-100, and treatment was started with .02 ml intradermally of this concentration. Details of treatment using these complexes will be reserved for a later report.

TABLE III. THE PATIENTS AND THE TESTS

Age range:	30-79 years
Average age:	58 years
Tested with both old and new series:	16
Old series (BAC 1, 2, 3, 4, 7, 8)	29 patients tested only to these.

RESULTS

The type of skin-test reactions produced by BAC given intradermally is shown in Figure 1.

The average age of these male veterans was fifty-eight years, although they ranged from thirty to seventy-nine years. Sixteen patients were tested to both the old and the new series. Twenty-nine patients were tested only to the old series (Table III). The number of patients tested to part or all of the new series, as these complexes became available, is shown in Table IV. It should be noted that 165 patients (58 per cent) in the series were tested to all five bacterial antigen complexes.

TABLE IV. NEW SERIES

BAC	Number Patients Tested	Per Cent
Pooled stock no. 1 only	5	2
Pooled stock no. 1 and no. 2	30	11
Pooled stock no. 1 and no. 2 and gram neg.	5	2
Pooled stock no. 1, no. 2, gram neg. and resp.	77	27
Pooled stock no. 1, no. 2, gram neg., resp. and staph.	165	58
Total	282	100

The skin reactions to bacterial antigen complexes which produced no change in the patients' symptoms differed in no way from those that did.

The amount of erythema, although measured, is not included because we agree wholeheartedly with Gottlieb, et al[3] that the degree of erythema is not proportional to the size of the wheal and is considered to be related to the patient's vasomotor status and skin pigmentation rather than to any immunological response (Table V). A comparison of the size of the delayed reactions in these two groups also showed little difference (Table VI).

TABLE V. TESTS—IMMEDIATE REACTIONS

	Wheal Size	Average
Responding to one or more BAC (to particular complex)	.5-1.7cm	.98cm
Not responding to any BAC (to all used complexes)	.7-1.4cm	.96cm

In those patients where there was improvement in the specific symptoms from one or more of the complexes, the skin test reactions, both immediate and delayed, were compared to the skin test reactions produced by the other complexes which had caused no change in symptoms. A comparison of the patients' symptomatic responses to the immediate and delayed skin test reactions indicated that there was more disparity than correlation (Table VII).

TABLE VI. TESTS—DELAYED REACTIONS

In those responding to one or more BAC, the skin reaction to the particular complex versus average reaction when there was no response to any BAC

	Responders		Non-Responders	
Less than 5mm	17	(8%)	7	(7%)
5mm	91	(45%)	45	(43%)
10mm	57	(28%)	40	(38%)
15mm	29	(14%)	12	(12%)
20mm	10	(5%)	0	
Total	204		104	

DISCUSSION

It has long been known by most allergists that little information could be gained through bacterial or vaccine skin tests.[7,10,12] Those who have believed in the reliability of these tests have undoubtedly, at times, used valueless vaccines, when perhaps the one which might have resulted in patient improvement was rejected.

TABLE VII. AGREEMENT OF SKIN TEST WITH PATIENT RESPONSE

Agree—BAC to which patient showed response gave larger skin reaction than to other BACs

	Immediate Reaction		Delayed Reaction	
Agree	84	(41%)	107	(52%)
Disagree	122	(59%)	99	(48%)

Tillett and Francis[11] demonstrated the type-specificity of the immediate skin test reaction to the various pneumococcal polysaccharides and their usefulness for the selection of immune sera for treatment. Julianelle and Wieghard[6] showed similar direct-immediate reactions to staphylococcal polysaccharides which were group-specific. A fair correlation of patient reaction versus skin test reactivity to individual strain and type Bacterial Antigen Complexes was apparently obtained in a small group of patients

with infectious asthma in an investigation conducted in the Allergy Clinic of Flower and Fifth Avenue Hospital in 1946.[5]

Even though acellular bacterial antigen complexes differ greatly from vaccines, the polyvalent bacterial antigen complexes react similarly. Although both immediate and delayed skin reactions were noted and measured, the largest reaction showed no more than chance correlation with the particular complex or complexes producing either improvement or exacerbation of the patient's symptoms.

It is realized that the bacterial antigen complexes used were pooled rather than a purified homogeneous antigen, but to use each organism as a separate test would be even more time consuming. Skin reactions to purified bacterial antigens have always been of questionable value, and there is no reason to believe that bacterial antigen complexes would produce more valid information.

SUMMARY AND CONCLUSIONS

In testing with bacterial antigen complexes which are acellular, colorless, clear, complete solutions of bacterial antigens, endotoxins and exotoxins of various combinations of organisms, there apparently is no correlation between immediate or delayed skin test and patient reaction.

ACKNOWLEDGMENT

The authors wish to express their appreciation for the assistance of Freeland G. White, E. E. Bartley, Richard T. Barrett and Phyllis J. Burdge.

REFERENCES

1. Editorial: Fiftieth anniversary of allergy. J Allergy, 27:383 (July) 1956.
2. Flensborg, E. W.: Infective allergy: A common factor in children's asthma, especially during infancy. Acta Allergol, 3:66 1950.
3. Gottlieb, P. M., Stupniker, S., and Askovitz, S. I.: The reproducibility of intradermal skin tests: a controlled study. Ann Allergy, 18:949 (Sept) 1960.
4. Gundy, John E.: Acellular bacterial antigen complex (Hoffmann) in the treatment of children with recurrent respiratory infections and infectious asthma. J Pediat, 5:516 (Nov) 1957.
5. Hoffmann, J. and Schulman, P. M.: Preliminary report on a group of cases of infectious asthma, treated with bacterial antigen complex (BAC) prepared from bacteria commonly found in the upper respiratory tract. Presented at a meeting of the staff (Allergy Clinic), Flower and Fifth Avenue Hospital, New York, N. Y., October 22, 1946.
6. Julianelle, L. A. and Wieghard, C. W.: The immunological specificity of staphylococci. J Exp Med, 62:11, 1935.
7. Scherago, M.: Bacterial allergy. Ann Allergy, 5:1 (Jan-Feb) 1947.
8. Shinefield, M. A.: The use of autogenous accelular bacterial antigen complex in the treatment of recurrent respiratory infections and asthma in infants and children. New York J Med, 56:1466 (May 1) 1956.
9. Spielman, Aaron D.: Treatment of infectious asthma and respiratory infections with acellular bacterial antigen complex. New York J Med, 55:1603 (June 1) 1955.
10. Swineford, Oscar J.: Observations on the use of bacterial antigens in the treatment of asthma: a brief critical review. Amer Practit, 1:612 (June) 1950.
11. Tillett, W. S. and Francis, T., Jr.: Cutaneous reactions to the polysaccharides and proteins of pneumococcus in lobar pneumonia. J Exp Med, 50:687, 1929.
12. Walker, I. C.: Clinical study of 400 patients with bronchial asthma. Boston Med Surg J, 179:288, 1918.

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SYMPTOMATIC BENEFIT FROM HOMOCHLORCYCLIZINE IN URTICARIA AND ANGIOEDEMA

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THE THESIS that histamine can produce urticaria seems to be well supported by laboratory and clinical data. The triple response of Lewis[1] follows the intracutaneous administration of the chemical (histamine). Moreover, histamine-releasing agents may cause pruritus, urticaria, and angioedema.[2] Mast cells, which contain histamine (as well as heparin and other physiologically active agents), are reported to decrease in the presence of urticaria; conversely, whealing areas of skin are said to have a lowered histamine content.[3] In addition, the patient with urticaria reportedly has an accompanying decrease in basophils—cells which are considered by many to be the equivalent in blood of mast cells in the tissues.[4]

At the clinical level, compounds which block histamine by competitive occupation of cell receptor sites, are often beneficial in the treatment of acute urticaria and angioedema.

While there is evidence for a direct histamine-urticaria relationship, it is not as decisive as we would like. Van Arsdel and Beall,[5] in a review of the physiologic roles played by histamine, observe that "even the relatively clearcut examples of histaminic effects are supported mainly by observations on the exaggerated responses to exogenous histamine administration."

One reason why it is difficult to obtain clear-cut proof that histamine is the sole precursor of urticaria is that there are few, if any, drugs which produce a "pure" antihistamine effect. When a patient responds favorably to an antihistaminic agent, there is a possibility that sedating or tranquilizing effects of the drug may contribute to the clinical result. This complicating factor cannot be ignored, because sedating and tranquilizing drugs are, *per se*, beneficial in urticaria and angioedema. The influence of the nervous system is also seen when clinical benefit follows the use of a placebo, and it is accepted that psychologic factors may perpetuate the chronic lesion.

When we study models of antigen-antibody reactions in the guinea pig, we find that a number of substances other than histamine are released, and several of these could cause or contribute to allergic skin lesions, e.g., bradykinin, "permeability factors," acetylcholine and serotonin. The last two substances are certainly capable of causing skin lesions. Hence "cholinergic urticaria" occurs in some individuals following excessive exposure to heat, or to psychic stress.[6] Furthermore, anticholinergic drugs are effective in some

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Presented at the Seventeenth Annual Congress of The American College of Allergists, March 15, 1961 at the Statler-Hilton Hotel, Dallas, Texas.

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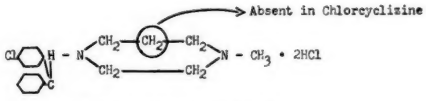
cases of hyperhydrosis,[7] another example where nervous-system-mediated effects (parasympathetic imbalance) are reflected in the skin. As for serotonin, this neurohumor substance is also a histamine-releaser,[8] (although its action in this regard is "weak" compared to that of 48/80). The subcutaneous administration of 5-hydroxytryptamine (serotonin) in the rat is followed by intense vasodilation and associated itching.[9] Either serotonin or histamine introduced locally into the rat's paw leads to anatomically indistinguishable edema, and prevention requires the specific antagonist, which is respectively dibenamine (for serotonin), or an antihistamine (for histamine).[10]

These circumstances may be only coincidental, but we cannot exclude the possibility that these substances, by acting in conjunction with histamine, could contribute to the urticarial lesions in man.

In nature, there are several examples of the simultaneous presence of histamine, acetylcholine and serotonin in itch-producing or pain-producing* biologic substances. Nettle stings contain high concentrations of all three.[11,12] Wasp venom contains both histamine and serotonin.[13] "Itch powder" (cowhage) contains a histamine-liberating substance, but also serotonin, as well as a proteolytic enzyme, mucunain.[14-16]

Whatever single or multiple mechanisms may be involved in the "allergic" skin lesion such as pruritus, urticaria and angioedema, it seemed worthwhile to study an agent which blocks several of the biochemical mediators. Homochlorcyclizine ("SA-97") is an agent which blocks both histamine and serotonin and is, in addition, weakly anticholinergic. Chemically this agent is a homologue of the well-known antihistamine chlorcyclizine. The structural formula demonstrates that the only difference between the two compounds is in the heterocyclic ring structure, where the six-membered piperazine nucleus of chlorcyclizine is replaced by the seven-membered homopiperazine nucleus of homochlorcyclizine.



"SA-97" - Homochlorcyclizine

This molecular change results in an enhancement of antiserotonin activity up to five times that of the parent compound chlorcyclizine, and at the same time, the original antihistamine activity is not decreased. The complete pharmacologic spectrum of homochlorcyclizine has been reported by Kimura et al.[17]

SA-97 was administered to thirty-eight patients, the majority of whom suffered from chronic urticaria and recurrent angioedema. The study has been conducted over the course of fifteen months.

*Pain has been described as a higher-intensity equivalent of itch.

METHOD OF STUDY

A preliminary study on a small series of ten patients served to test a double-blind procedure. This group consisted of nine patients with long-standing urticaria (and one with fairly recent urticaria following penicillin). In seven of the cases, no previous therapy had been given; in the remaining three, pre-existing medication was stopped. Tablets of SA-97 (A) and of placebo (B) were prepared. The observers were unaware of the identities. No changes in diet or environment were made. The two unknown tablets were administered in random sequence to four patients, but either A or B alone was given to the remaining six. Table 1 demonstrates the results, and also the reason why it became clear to the "blind" investigators that Tablet A was SA-97 and Tablet B was placebo.

TABLE I. FIRST SERIES—"DOUBLE-BLIND" PROCEDURE
Ten Cases

Patient's Age and Sex	Condition Treated	Treatment*	Results
45 F	Giant urticaria	(1) B—7 days	Fair
	Angioedema	(2) A	Excellent
10 M	Chronic urticaria	(1) A—2 weeks	Excellent
		(2) B—10 days	Fair to no relief
12 M	Chronic urticaria	(1) B—2 weeks	Fair
		(2) A	Excellent
37 M	Acute hives	(1) Prednisone 2 days	No relief
		(2) A	Complete relief same day
30 M	Chronic urticaria	B—7 days	No relief**
30 F	Chronic urticaria	A	Complete relief
45 F	Chronic urticaria	B—7 days	No relief**
12 M	Giant urticaria	(1) B	No relief in 3 hours
		(2) A	Urticaria subsided in 20 min.; disappeared in 3-6 hrs.
12 M	Chronic urticaria	(1) Trimeprazine 2 years	Fair
		(2) A	Complete relief in few days
40 F	Chronic urticaria	(1) Trimeprazine 6 months	Good
		(2) DC Trimeprazine 6 days	Return of urticaria
		(3) A	Complete relief

*A = Real drugs. B = Placebo.
**Tablet A not available for this case.

Consequently a second series of twenty-eight cases was started under "single-blind" conditions, i.e., the patients were alternated (whenever feasible) between successive periods of SA-97 and an identically-appearing placebo. While the patients were not aware of the change in medication, the clinician was. These patients suffered from recurrent urticaria or angioedema, and were selected on the basis of their known response to previous medication such as well-known antihistamine, phenothiazine, or steroid drugs. Unsatisfactory response, or failure, or "accommodation" to those agents had been observed to occur in some. In a few, the response was deemed to have been "good." The response to previous medication served as a baseline to assess the response to homochlorcyclizine.

Criteria were the subjective relief of itch, and the objective disappearance of the lesions.

RESULTS

Benefit from SA-97 ranked from "excellent" to "good"** with the majority of cases falling into the first category. In every case where both drug and placebo were employed, there was a clear and marked difference. When homochlorcyclizine was replaced by the placebo, relapse invariably occurred. Return to the real drug was followed by reappearance of the earlier response. When compared to other types of agents previously used by the same patients, homochlorcyclizine was judged to produce superior results in twenty-one cases, and equally good results in the remaining seven cases. In nine cases where steroids had been employed previously, the results were considered to be equally satisfactory, and steroid medication was not required while homochlorcyclizine was in use.

Table II lists the characteristics of these patients, their previous regimens, their comparative responses, and other pertinent observations or comments.

DISCUSSION

While the results from homochlorcyclizine were judged to be superior to those obtained from the previously used antihistamines or tranquilizers, we cannot attribute the key pharmacologic effect to any one of the several actions of this drug. We can speculate that possibly more than one pharmacologic action proved to be beneficial in these cases, i.e., antihistamine, antiserotonin, anticholinergic, and/or psychotropic actions—all of which are possessed by SA-97 in varying degrees.

Previous clinical studies with homochlorcyclizine have been primarily concerned with its effectiveness in respiratory allergy. Fisherman *et al*[18] found it to be a useful adjunct in bronchial asthma and allergic cough, et cetera, but also reported "good" or "excellent" response in twenty out of twenty-four cases of urticaria and angioedema out of a total of 346 cases having allergic symptoms of various types. These investigators commented that the effectiveness of this agent could not be explained by its "known antagonism to histamine, acetylcholine, or serotonin or by simply bronchodilator action." In another investigation[19] limited to respiratory allergy, results were only mediocre. But the lack of benefit from antihistaminic agents is well known in bronchial asthma, and further, the absence of serotonin in human lung[20] would seem to make it unlikely that the addition of antiserotonin to antihistamine properties in a single drug would result in additional benefit. Yet, in the skin, where serotonin is equally scarce (human), the combination of antihistamine and antiserotonin actions appears to be effective for treatment of pruritus, urticaria and angioedema. In this connection, attention is drawn to recent reports of similar benefit following the use of cyproheptadine[21,22] which has pharamcologic properties similar to those of homochlorcyclizine.

**Rating scale (see Tables I and II): Excellent—no urticaria; Good—very little urticaria; Fair—some alleviation; Poor—no improvement.

TABLE II. SECOND SERIES—"SINGLE-BLIND" PROCEDURE
Twenty-eight Cases

Patient's Age and Sex	Present Skin Symptoms and Duration	Previous Therapy*	Other Allergic Signs (and Therapy Therefor*)	Effect on Skin Symptoms Associated with							
				SA-97**				Placebo			
				E	G	F	P	E	G	F	P
36 F	Urticaria, 3 months	AH, TR	None	X							X
11 M	Urticaria, angioedema, 4-5 recurrences for 1 year	PT	Allergic rhinitis, 6 months (hyposen.—food exclusion)	X							X
6 F	Urticaria, 6 months	AH	None	X							X
5 M	Urticaria, angioedema, recurred for 1 yr.	AH	Allergic rhinitis, 2 years (AH)	X				N	ot	use	d
10 M	Urticaria, angioedema, 6 months	AH, PT	Allergic rhinitis, asthma—5 years (hyposen.) (AH's)	X							X
14 F	Urticaria, 6 months	PT	Allergic rhinitis, 2 years (AH's)	X							X
38 M	Urticaria, 6 years	PT	Allergic rhinitis, 10 years (hyposen.)	X							X
45 F	Urticaria, 6 weeks	S, PT, AH's	None	X							X
2½ M	Urticaria, eczema, 2 weeks	AH	None	X							X
5 M	Eczema, chronic	PT, S	Asthma (S, BD)	X				N	ot	use	d
2½ F	Eczema, 2 months; urticaria, 1 month	PT, S	None		X						X
40 F	Urticaria, angioedema, 6 weeks	S	None	X							X
18 M	Urticaria, 2 days	AH	Allergic rhinitis, 10 years	X							X
26 F	Urticaria, 5 years	AH	Eczema, 5 years (S topical)		X						X
20 F	Urticaria, recurred for 3 yrs. (present episode—6 weeks)	PT, AH, S	Allergic rhinitis, 6 years (AH)	X							X
15 F	Urticaria, 3 years; eczema, chronic	AH	Asthma, 10 years		X						X
4½ F	Eczema, 2 years	PT, S	None	X							X
1 M	Urticaria, eczema, 2 months	PT, S	None		X						X
30 F	Urticaria, 6 months	PT, AH	None	X							X
11 M	Urticaria acute, angioedema, 1 week	PT, ACTH	Allergic rhinitis, bronchitis, 2 years (AH, VC)	X							X
29 M	Urticaria, 1 week		None		X						X
17 F	Urticaria, 6 months	PT, AH, S	Allergic sinusitis	X				N	ot	use	d
40 F	Eczema, pruritus, 20 years	PT, S	None	X							X
38 F	Seborrheic derm., urticaria, 3 months	Selsun, PT	None		X						X
6 M	Urticaria, 2 weeks		Bronchial asthma, 2 years	X							X
24 F	Urticaria, 5 months	AH, S	Allergic rhinitis, 10 years		X						X
11 F	Urticaria, 3 months	PT, AH	None	X					X		
12 M	Urticaria, 4 months	AH	Allergic rhinitis, 2 years	X							X

*AH=antihistamine (i.e., diphenhydramine, parabromdylamine, diphenylpyraline, chlorphenhydramine); TR=tranquilizer; PT=phenothiazine, usually trimeprazine; S=steroid; VC=vasoconstrictor; BD=bronchodilator.
**25 mg q.i.d.—adult dose.

The number of variables in the response to the treatment of itching dermatoses is so great that the high rate of success in this (or any) study must be viewed cautiously. We presume that a larger series might disclose a more realistic (lower) response rate. In three patients it was noted that control of subsequently recurring lesions required five or six tablets of SA-97 in order to effect the same benefit obtained initially with one or two tablets. These and other aspects require extended study.

SUMMARY

Homochlorcyclizine (SA-97) possesses several pharmacologic properties including antihistamine and antiserotonin activity.

Clinical observations have been made on thirty-eight patients who received homochlorcyclizine for treatment of urticaria and angioedema. Results were compared with the previous benefit, or lack of it, obtained from therapeutic agents previously employed by the same patients, i.e., drugs having anti-pruritic, anti-histaminic, or anti-inflammatory (corticosteroid) action. In twenty-nine out of the thirty-eight patients, results were also compared with those obtained from an identically-appearing placebo.

The results from SA-97 were always superior to those from the placebo. In the nine patients where no comparison with placebo medication was made, the results were similarly favorable.

Results from SA-97 were also judged to be better than those obtained previously when these same patients employed antihistamine, tranquilizer, or steroid therapy.

While this investigation indicates that homochlorcyclizine is a useful agent for relief of pruritus, urticaria and angioedema, its mechanism of action cannot be clearly defined.

REFERENCES

1. Lewis, T., Grant, R. T., and Marvin, H. M.: Vascular reactions of the skin to injury; intervention of a chemical stimulus illustrated especially by flare; response to faradism. Heart, 14:139, 1927.
2. Paton, W. D. M.: Compound 48/80: A potent histamine liberator. Brit J Pharmacol, 6:499, 1951.
3. Kanof, Norman B.: Urticaria. Med Clin No Amer, 43:779, 1959.
4. Rorsman, H.: quoted in reference 3.
5. Van Arsdel, Paul P., Jr., and Beall, Gildon, N.: The metabolism and functions of histamine. AMA Arch Intern Med, 5:714, 1960.
6. Garretts, Maurice: Cholinergic "urticaria" and miliaria. Brit J Derm, 70:166, 1958.
7. Hamilton, William: The control of hyperidrosis. The Medical Press, 240:962, 1958.
8. Feldberg, W. and Smith, A.: Release of histamine by tryptamine and 5-hydroxytryptamine. Brit J Pharmacol, 8:406, 1953.
9. Erspamer, V.: Observations on alleged serotonin—(Enteramine)—like nature of cerebral pressor substance of Taylor, Page and Corcoran. Arch Intern Med, 90:505, 1952.
10. Rowley, Donald A. and Benditt, Earl P.: 5-Hydroxytryptamine and histamine as mediators of the vascular injury produced by agents which damage mast cells in rats. J Exp Med, 103:399, 1956.
11. Emmelin, N. and Feldberg, W.: Mechanism of sting of common nettle (Urtica urens). J Physiol, 106:440, 1947.

12. Collier, H. O. J. and Chesher, G. B.: Identification of 5-hydroxytryptamine in the sting of the nettle (urtica dioica). Brit J Pharmacol, 11:186, 1956.
13. Jaques, R. and Schachter, M.: Presence of histamine, 5-hydroxytryptamine and potent, slow-contracting substance in wasp venom. Brit J Pharmacol, 9:53, 1954.
14. Broadbent, J. L.: Observations on itching produced by cowhage, and on part played by histamine as mediator of itch sensation. Brit J Pharmacol, 8:263, 1953.
15. Bowden, K., Brown, B. G., and Batty, J. E.: 5-hydroxytryptamine: Its occurrence in cowhage. Nature (Lond), 174:925, 1954.
16. Shelley, W. B. and Arthur, R. P.: Studies on cowhage (Mucuna pruriens) and its pruritogenic proteinase, Mucunain. Arch Derm Syph, 72:399, 1955.
17. Kimura, Eugene T., Young, Patrick R., and Richards, Richard K.: Pharmacologic properties of N-p-Chloro-Benzhydryl-N'-Methyl homopiperazine dihydrochloride (Homochlorcyclizine: SA-97), A Serotonin Antagonist. J Allergy, 31:237, 1960.
18. Fisherman, E. W., Feinberg, S. M., Feinberg, A. R., and Pruzansky, J. J.: Homochlorcyclizine: an antiallergic drug with multiple clinical properties. J Allergy, 31:232, 1960.
19. Arbesman, C. E., and Ehrenreich, R. J.: New drugs in the treatment of allergies. New York J Med, 61:219, 1961.
20. Undenfriend, Sidney and Waalkes, T. Phillip: On the Role of Serotonin in Anaphylaxis. Mechanisms of Hypersensitivity (Henry Ford Hospital International Symposium). Boston: Little, Brown and Company, 1959.
21. Miller, Jerome and Fishman, Aaron: A serotonin antagonist in the treatment of allergic and allied disorders. Ann Allergy, 19:164, 1961.
22. Welsh, Ashton L. and Ede, Mitchell: Efficacy of cyproheptadine as an antipruritic agent: a preliminary report. J New Drugs, 1:22, 1961.

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I HAVE DONE WHAT I COULD

"Whatever your career may be, do not let yourselves become tainted by a deprecating and barren scepticism. Do not let yourselves be discouraged by the sadness of certain hours which pass over nations. Live in the serene peace of laboratories and libraries. Say to yourselves first: 'What have I done for my instruction?' and, as you gradually advance, 'What have I done for my country?' until the time comes when you may have the immense happiness of thinking that you have contributed in some way to the progress and to the good of humanity. But, whether our efforts are or not favoured by life, let us be able to say, when come near the great goal, 'I have done what I could'."—BENJAMIN BOSHES, M.D., Ph.D., "Live in the Serene Peace of Laboratories and Libraries," Pasteur, (*Quart Bull Northw Univ Med Sch,* 34:286, Winter, 1960).

LIGHT SENSITIVITY TREATED BY HYPOSENSITIZATION

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THE effects of sunlight on the skin have been discussed previously;[1,2,3] this report does not concern itself with sunburn in normal skin, but with an abnormal reaction to daylight exposure, wherein subjective burning and itching and objective erythema and vesiculation result from an exposure to an amount of sunlight far smaller than that required to produce visible skin changes in a normal person.

The literature has offered little for the treatment of this condition. In a discussion of diseases related to light sensitivity, Kesten and Slatkin[4] offer topical ointments only. Lamb et al[5] discuss hormonal therapy and Atabrine for solar dermatitis manifested as hyperkeratosis and parakeratosis. Duke[6] employed a series of exposures to ultraviolet light in an attempt to desensitize his patient, with negative results. Hurst,[7] on the other hand, claimed a cure for light sensitization by progressive light desensitization. Both workers, as well as Scott and Molhuysen,[8] employed doses of over one minute duration of ultraviolet light. In this report, the effects of many more doses than employed by the authors noted, in amounts much smaller than those previously employed, will be evaluated. It was believed that small doses would avoid formation of plaques of hyperkeratosis noted from much larger doses administered by Lamb et al.[5]

An example of abnormal light sensitivity (probably an eczematous example of the so-called polymorphous light eruption) is presented, with a course of treatment pursued and an evaluation of its success.

CASE REPORT

The patient, aged forty-five years, is a nun and a parochial school teacher. Her past history showed an allergic background, which included migraine, Meniere's syndrome, allergic rhinitis, and allergic bronchitis between 1953 and 1960. A number of skin tests had shown moderate reactions to a few antigens.

In the summer of 1960, she first noticed that when she went out of doors, she developed redness and tiny vesicles and itching on her hands and face, progressing in severity as the summer advanced. The style of her dress—the type of habit including band across the forehead and coif around the face—was such that only her hands and her face exclusive of neck and upper forehead were exposed to light. When she first sought medical help for this condition, hydrocortisone ointment was prescribed for the folliculitis-like tiny vesicles which were observed at that time. At her next clinic visit, edema was also observed on those areas of her face and hands exposed to light. She was hospitalized for twelve days and received steroid hormones and antihistamine, with resultant clearing of the dermatitis. During this hospitalization, she noted that she developed burning and itching of the face and hands when she sat in a chair by the window where sunlight fell upon her. This

would indicate that ultraviolet rays of wave length longer than 3200 Ångstrom units were responsible for her symptoms.

She was readmitted to the hospital for five days because of a recurrence of edema and erythema of the exposed portion of her face only. She now had no involvement of her hands; she had faithfully been wearing gloves on the automobile rides to and from her school, which was the only time she was out of doors. This time, Burrow's solution packs were employed, as well as the previous treatment. She returned to the hospital with the same clinical picture.

In seeking causes of light sensitivity,[4] experimenters found no LE cells on her blood smear which was done on two different occasions. Urine was negative for porphobilinogen; WBC 4800, with neu 70, lym 28, mon 1, bas 1. The urine was negative for coproporphyrins. Of the drugs listed by Sams[9] which may cause photosensitivity, the only one she had ever received before her development of light sensivity was a brief course of a sulfonamide in April, 1956, and she had received no more sulfonamides since then.

An attempt was made to desensitize her to sunlight by giving progressive daily exposures of ultraviolet light. A conservative dose of only three seconds was started, at thirty-six inches distance, using an air cooled quartz mercury vapor lamp.[10] If any effect was noted from the day's dose (erythema, itching, burning, vesiculation, edema), that day's dose was repeated the next day; if no effects were noted by the patient, the dose was increased the following day. The effects were noted typically in the evening. The regime pursued resulted in her receiving two doses of three seconds, six seconds, and ten seconds, respectively, one dose of fifteen seconds, and three of twenty-five seconds. Following this regimen, a daily dose of forty seconds was found to control her symptoms. After five daily forty-second doses, the ultraviolet exposures were discontinued.

It was later noted that she had been able to go out of doors without discomfort since her last discharge from the hospital, but subsequently she had noticed some symptoms in the evenings of those days she had been out of doors. A second series of ultraviolet exposures, therefore, was given. It was noted that the exposure could be started at a higher dosage and increased more rapidly than in the first series. This time two daily doses of ten seconds, then two of fifteen seconds were given. After a weekend, two doses of twenty-five seconds and one of forty seconds were given on consecutive days. It was decided to give her a weekly maintenance dose thereafter. Because of a lapse of a week's time, a dose lasting only thirty seconds was given. No reaction occurred from this. Subsequently, the patient was out of doors for one and one-half hours, far longer than she had been for months; she developed only a slight redness that evening. The next week's dose of thirty seconds produced no effect, so the following week a forty second-dose was given. Some redness resulted that evening, and forty seconds were repeated thereafter. A dose of forty seconds now produced no effect, and this dose was given at bi-weekly intervals. Light sensitivity has not recurred on this bi-weekly treatment at the time of this writing.

CONCLUSION

Judging from this case, it may be feasible to increase the light tolerance in a patient who is allergic to light by a method somewhat analogous to desensitization to inhalants through periodic injection of progressive doses of antigens . . . that is to say, by periodic exposures to progressive doses of ultraviolet light.

REFERENCES

1. Kesten, B. M.: Effects of sunlight on the skin. JAMA, 161:1565, 1956.

2. Duke, W. W.: Urticaria caused specifically by the action of physical agents. JAMA, 83:3, 1924.
3. Duke, W. W.: Physical allergy. JAMA, 84:736, 1925.
4. Kesten, B. M. and Slatkin, M.: Diseases related to light sensitivity. Arch Derm & Syph, 67:284, 1953.
5. Lamb, J. H., Jones, P. E., and Maxwell, T. B.: Solar dermatitis. Arch Dermat, 75:171, 1957.
6. Duke, W. W.: Urticaria caused by light. JAMA, 80:1835, 1923.
7. Hurst, A.: Light sensitization cured by progressive light desensitization. Practitioner, 141:220, 1938.
8. Scott, F. P. and Molhuysen, S. M.: Light dermatoses. Dermatologica, 116:96, 1958.
9. Sams, W. M.: Photosensitizing chemotherapeutic agents. JAMA, 174:2043, 1960.
10. Krusen, F. H.: Physical Medicine. p. 187. Philadelphia: W. B. Saunders Co., 1941.
11. Beal, P. L.: Studies in solar urticaria. J Invest Dermat, 11:415, 1948.

221 5th Street

ALLERGY FOUNDATION OF AMERICA FELLOWSHIP IN ALLERGY

The Scientific and Educational Council of the Allergy Foundation of America has selected Dr. Henry N. Claman for the Burroughs Wellcome Fellowship in Allergy. Doctor Claman will work with Dr. David W. Talmage, Professor of Medicine and Microbiology at the University of Colorado School of Medicine.

Doctor Claman, a thirty-one year old physician, is a graduate *cum laude* of Harvard College where he majored in philosophy. He entered New York University College of Medicine and received in 1955 his degree as an M.D. He interned and was an assistant resident at Barnes Hospital, St. Louis, Missouri, from 1955 to 1957. He thereafter served as a resident in medicine for two years at the Massachusetts General Hospital, Boston, Massachusetts. Beginning early in 1961, he began to work in the research laboratories of the University of Colorado Medical Center and under the guidance of Doctor Talmage.

ALLERGIC TREMOR

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and BRAHAM J. GEHA, M.D.
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ALLERGIC REACTIONS of the central nervous system and convulsive disorders due to allergic disease have been documented.[1-3] Few references are made to tremors of localized limbs due to allergies. Clark and Rosenberg described a case of atonic seizures of the upper extremities associated with Loeffler's syndrome due to ascaris.[4] A patient with muscular contractions and lethargy associated with urticaria was seen by Crowe.[5] Davison mentioned twitching as a symptom of central nervous system allergy in two classical articles on the subject.[6,7] In most cases of convulsive disorder associated with allergic disease of the central nervous system which have been described there is an associated allergic disease of the respiratory tract or skin.

Considerable discussion has been devoted to nervousness or behavior problems in allergic individuals. This has been described variously as "allergic toxemia," "allergic shock" or "allergic tension."[8,9] This terminology, which to a great extent is interchangeable, records a hyperkinetic behavior pattern. Frequently, this type of behavior changes considerably with the control of the allergic symptoms. Much debate has occurred on the true existence of this clinical picture and whether it is due to a nonspecific effect on the individual or possibly to a specific effect on the central nervous system itself giving rise to such symptoms. There has been a wide divergence of opinion on the incidence of abnormal encephalograms in allergic children.[10-13]

The authors wish to present a case of a tremor associated with allergic respiratory disease and controlled by allergic management. The tremor could be reproduced by feeding, injecting or breathing the known allergens.

CASE REPORT

D. C. is a seven-year-old boy with rhinitis, asthma, tremor of all extremities and nervousness. The respiratory symptoms began at age three; were worse from spring to frost, around cats and dogs, during storms and wind and ingestion of chocolate. The patient was born two months prematurely and spent six weeks in an incubator. He walked at eleven months and other developmental features were normal. The tremor was present in all extremities but worse in the arms, and particularly massive twitching occurred over the right biceps and right shoulder. The boy has always been nervous. He has been an average scholar. At age five, a neurological and fundoscopic examination, disclosed completely negative examination, normal skull x-rays and an abnormal encephalogram with slow waves. The diameter of the skull was 51.9 cm (normal). A diagnosis of "idiopathic tremor" was made.

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Presented at the Seventeenth Annual Congress of The American College of Allergists, March 17, 1961, Statler-Hilton Hotel, Dallas, Texas.

The mother noted that although dilantin controlled the tremor, antihistamines gave quicker and better results. The tremor was increased with fatigue and excitement and there was marked nocturnal myoclonus. There were no actual convulsions.

His father suffered from hay fever and his mother had a skin sensitivity due to chocolate.

The patient was found to be extremely sensitive to ordinary house dust, fungi spores, grain mill dust, bacteria, cat and dog hair, grass and ragweed pollens and to chocolate. When given in a low dosage of 0.1 cc of 1:35,000,000 these inhalent antigens completely controlled the symptoms. However, when the dosage was increased by 50 per cent, the tremors began within ten minutes and lasted for two days unless antihistaminic agents were administered. This was repeated several times without the patient's or his mother's knowledge. Chocolate, respiratory infections and ragweed pollen exposure promptly caused some tremors. After one year of allergic management which consisted of avoidance and hyposensitization, both the tremor and the respiratory symptoms improved considerably. Then, electroencephalograms were taken before and after the ingestion of four ounces of chocolate. Both of these tracings were reported as normal. However, thirty minutes after he ate the chocolate, the boy stated that he felt "nervous," and fifteen minutes later, atonic twitching began in the left arm and rapidly spread first to the right arm and then to both legs. The mother reported that after antihistaminic agents were taken, the tremors stopped in twenty-four hours.

COMMENT AND SPECULATION

The basic patho-physiologic effect in allergic reactions is local vasodilation and increased capillary permeability with a resultant localized edema. Such a lesion is commonly seen in the conjunctival membrane, nasal mucosa and bronchial wall. Theoretically, such a process could occur in the nervous system leading to edema. This edematous brain lesion has been seen at surgery on two occasions, by Kennedy with a preoperative diagnosis of brain tumor and Barsoe with a preoperative diagnosis of brain abscess.[14,15] Criep reported vertigo as the probable result of an allergically induced edema of the inner ear.[16]

Occipital slowing of the electroencephalogram has been reported in children with allergy. An abnormal electroencephalogram at age five and the inability to precipitate this after allergic stimulation are interesting observations which do not support the theory of a local lesion. Treatment may have been responsible. Stimulation of the reticular system of the brain stem alters the state of consciousness, and it is thus possible that an allergic process could cause hyperkinesia by excessive stimulation of this structure or by temporary damage of its pathways.

In this case, the patient and his family knew of many of the factors which precipitated both the respiratory symptoms and the tremor, so that the element of suggestion could have been present. However, with the variation of dosage regulated with only the physician's knowledge, i.e., by means of a single blind test technique, such suggestion is ruled out. This is a valid point of many previous papers. In this case, the increase of the dose from 0.1 cc to 0.15 cc precipitated within ten minutes the tremor which lasted for two days unless relieved by an antihistaminic agent. The central

nervous system effects have been described as possibly due to the alkalosis secondary to bronchial asthma.[17] In this case, the tremor usually occurred without an asthmatic attack.

CONCLUSION

We have presented a case of a boy afflicted with allergic respiratory disease associated with a gross tremor of all extremities. The tremor has been controlled by allergic management. It is brought on by the ingestion, the inhalation or the injection of known allergens. Antihistaminic agents control the tremor better than dilantin. We have briefly reviewed the literature on convulsive disorders associated with allergic disease. Although this is the third case recorded of tremor associated with allergic disease, there may be many similar patients who can be helped with allergic management.

ACKNOWLEDGMENTS

We wish to thank Harold Lyddon, M.D., for his cooperation and his permission to discuss his patient. Our gratitude is extended to Dr. Robert Forsythe and Dr. E. H. Trowbridge for their records and Dr. Frederic Speer for his interest and assistance in preparing the data. We also wish to thank Dr. Dewey Zeigler for his assistance with the electroencephalograms.

REFERENCES

1. Pardee, Irving: Allergic reactions in the central nervous system: report of two cases. AMA Arch Neurol Psychiat, 39:1360, 1938.
2. Adamson, W. B. and Sellers, M.D.: Observations on the incidence of the hypersensitive state in one hundred cases of epilepsy. J Allergy, 24:315, 1933.
3. Spangler, Ralph; Allergic findings in epileptic patients and ancestors. Ann Allergy, 1:91, 1943.
4. Clark and Rosenberg as quoted by Glaser, Jerome: A critical review of recent literature, pediatric allergy. Ann Allergy, 6:178, 1948.
5. Crowe, W. R.: Cerebral allergic edema. J Allergy, 13:173, 1942.
6. Davison, Hal M.: Cerebral allergy. Southern Med J, 42:712, 1949.
7. Davison, Hal M.: Allergy of the nervous system. Rev Allergy, 6:157, 1952.
8. Speer, Frederic: The allergic tension-fatigue syndrome in children. Int Arch Allergy, 12:207, 1958.
9. Rowe, Albert H.: Allergic fatigue and toxemia. Ann Allergy, 17:9-18, 1959.
10. Dees, Susan C.: Neurologic allergy in childhood. Pediat Clin N Amer, 1:1017, 1954.
11. Panzani, R., Boyer, R., and Turner, M.: The electroencephalogram in migraine and asthma. Ann Allergy, 18:491, 1960.
12. Berman, Bernard A., Engel, George L. and Glaser, Jerome: The electroencephalogram in allergic children. Ann Allergy, 17:188, 1959.
13. Chobot, Robert, Dundy, Harold D., and Pacella, B. L.: The incidence of abnormal electroencephalographic patterns in allergic children. J Allergy, 21:334, 1950.
14. Kennedy, Foster: Cerebral symptoms induced by angioneurotic edema. AMA Arch Neurol Psychiat, 15:26, 1926.
15. Bassoe, Peter: The auriculotemporal syndrome and other vasomotor disturbances about the head. Med Clin N Amer, 16:405, 1932.
16. Criep, L. H.: Allergic vertigo. Pennsylvania Med J, 43:258, 1939.
17. Klein, J.: Allergic epilepsy. J Pediat, 3:505, 1933.

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Basic Briefs

THE PSYCHO-PHYSIOLOGIC APPROACH IN THE MANAGEMENT OF THE ALLERGIC PATIENT

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EACH OF US likes to describe his own therapeutic endeavors as a science, an art, or both. Our motives for so doing lie in our personal inclination and are determined to a large extent by our specific training and experience. We will not label our presentation, but will let you decide whether it is science, art, or fiction.

The thesis of this presentation is that our effectiveness as allergists could be greatly enhanced by the use of the psycho-physiologic approach since non-immunologic factors often decide the course and result of allergic management. This approach can be characterized as follows: (1) it considers the mutual interaction of physiologic and psychologic processes, (2) it recognizes the significance of emotional tension as one among several possible etiologic factors in the genesis and perpetuation of illness, (3) it shifts the focus of attention from the disease process to the sick person, (4) it appreciates that the reciprocal patient-doctor relationship is the medium in which all therapy occurs.

Thus, it should be clear that this approach is in no way a replacement for accepted allergic procedures. On the contrary, it embodies all the conventional methods but adds an additional body of information—the psychology of human behavior.

There is a tendency among many physicians to equate the psycho-physiologic approach with the practice of psychiatry. This confusion should not be allowed to persist. This presentation is not a discussion of psychiatry as a specialty, but is an endeavor to clarify the type of psychological understanding which the allergist can bring to bear in his everyday practice.

Just as electrical energy can produce light, heat, sound and motion according to the manner of its employment, so too can emotional energy produce behavioral, emotional and somatic effects. Nervous tension discharging into vasomotor, vasosecretory and other visceral channels can bring about a broad spectrum of metabolic and physiologic responses in-

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Presented at the Graduate Instructional Course of The American College of Allergists, March 14, 1961, at the Statler-Hilton Hotel, Dallas, Texas.

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cluding blood pressure changes, white count elevation and blood-sugar reactions. There is no one who has not at some time experienced with poignancy the physical reverberations of high emotional states: dryness of the throat, tremors, shaking of the knees, tachycardia and increased perspiration, to mention a few of the most common signs.

Although it can't be seen, emotional (like electrical) tension has an imperative reality. Its effects, mediated through the autonomic and endrocrine systems, are undeniable. Emotions, in a broad sense, can be etiologically significant in many functional disorders, can explain fluctuations in the intensity of symptoms, can influence the course and outcome of various dysfunctions and spell the difference between latent or manifest expressions of weakness in a particular organ system. We know also that certain physiological processes once set off on the wrong functioning path by powerful psychological forces can sometimes become irreversible and chronic.

Inevitably then, the question occurs as to how and why emotions, which are part and parcel of our normal development and daily lives, produce these untoward effects? It must be that the emotions themselves are not pathological, but rather it is the characteristic patterns by which we deal with them that are, in part, inimical to our health. In order to elucidate this point more fully, it is necessary to examine some fundamental concepts.

The most elemental human feelings are pleasure and pain. Each in his own way strives intrepidly to maintain that vastly complex orientation which concurrently strives to maximize pleasure and minimize pain. When circumstances impel a deviation from this course, we feel threatened and an alarm signal in the form of anxiety is triggered. The most primitive of our emotions is anxiety, which serves the maintenance of psychological homeostasis by these warnings. Anxiety can be associated with real external danger or, what is more commonly the case, with personal situations which we interpret as being potentially destructive to our personalities. Anxiety is therefore an emotional experience which can be useful and normal, serving to bring to our awareness potential hazards. Once a threat is perceived, anxiety motivates us to mobilize our defenses.

The pain of diffuse anxiety carries an urgency that can't be tolerated and evokes within the individual a need for immediate reaction to relieve this anguish. The initial awareness of a stimulus which is felt to be hostile stirs an almost simultaneous series of automatic defensive maneuvers which absorb the emotional energy invested in the anxiety and thereby affords partial relief from the discomfort associated with these reactions. It is this pattern of defensive mobilization that is the hallmark of the individual personality and determines the degree of effectiveness of one's over-all adjustment to life. This configuration of anxiety defenses is reflected in such aspects of personality as the types of character traits present, the kind and extent of neuroticism and the proneness to various psycho-physical disorders.

The personality may avail itself of three principal methods to cope with an intrusion of anxiety: *through behavior, through emotions* and *through psycho-physical reactions.* The method of choice will depend on a vast array of factors the description of which lies beyond the scope of this paper. Suffice it to say, these factors relate to a complex interaction of need and need-satisfaction patterns developed early in life with many currently operating situational influences.

Direct physical action against the provoking stimulus is the most primitive response one can make to anxiety. Most of us have had the experience of kicking back at an offending chair which "got in our way," or seen a woman take direct action by fleeing the vicinity of a threatening mouse. If neither course of behavior—fighting back or fleeing—is open to us, then random activity, such as the floor-pacing of the proverbial expectant father, serves both to distract and to provide an outlet for the anxious energy. Whichever course of action is chosen, however, the result is the same—the experience of the anxiety is mitigated and made easier to bear by translating it into activity.

Since the vicissitudes of life do not all lend themselves to the behavioral expression of emotion then, for the sake of effective adaptation, other channels must be available. The experience of anxiety can be more readily tolerated if the generalized emotion can be localized. Just as behaviorally we try to choose a specific object to strike against or flee from, so too, psychologically, we tend to choose a particular object or idea to react against. We find it simpler and less incapacitating to focus our defensive efforts against a single enemy and so to circumscribe the anxiety. As a consequence such symptoms as hysterias, phobias and obsessions are produced which are examples of the psychological translation of this elemental anxiety. Other higher-order emotions (like fear, rage, depression, longing, et cetera) are derivatives of anxiety also.

Still, a third means of coping with emotional stress remains to be considered—the somatization of anxiety. This mechanism of somatizing emotion with the resultant physical symptoms may be thought of as being on a higher level than the direct behavioral expression of feeling, yet more primitive than the psychological mechanisms. By this process the emotional experience of anxiety is transformed from psychologic to physiologic awareness. With the completion of this transformation, emotional stress (as such) no longer exists and, in its stead, there is an increased level of physiologic stress with all the possible attendant complications. One of these complications is a heightened susceptibility of compliant organs to react by dysfunction to this increased stress.

Unlike the other two types of emotional expression, the individual is totally unaware of that portion of anxiety which has become thus transformed. The only discomfort which exists is related to the somatic condition, consequently they are more emotionally at ease than persons utilizing the other mechanisms of anxiety defense. Emotional insight, however,

remains profoundly limited as long as the psychic energy remains so absorbed. The impulsivity of the behavior disorder and the anxious tension of the neurotic trait are readily discernible when compared with the relative emotional quiescence of the psycho-physical symptom. This fact may account for the prevalant incredulity regarding the significance of the psychological component in these conditions.

Obviously, not all human beings handle anxiety in the same way. Most choose some combination of these methods through which to absorb, divert or express tension. Once, however, these patterns are set up they tend to remain fixed. The emotional energy gets "locked-in," as it were, and the system becomes self-perpetuating.

Different reaction patterns are related to various levels of emotional maturity. Each developmental phase tends to have a predominant pattern of psychological adjustment associated with it. So as we grow, we give up more primary mechanisms as we adopt those which are more advanced. In this progression, the direct behavioral responses are the more primitive, and the emotional and intellectual responses the more advanced. At times of high frustration, the pressure of anxiety tends to drive us back to earlier ways of responding. This psychological moving backward is called regression. The phenomenon of regression occurs when we feel overwhelmed by difficulties—physical, emotional or environmental in our current life situation. We retreat to former lines of defense which were utilized in an earlier age. As we move back in psychic time, traces of former patterns are reactivated by the emotional energy of the anxiety. Progress from the broader perspective of greater maturity to the more contracted horizons of earlier levels of adjustment serves to consolidate our defense and conserve the energy reserve of our threatened ego.

It is possible, therefore, for psycho-physical conditions to exist without our being conscious of psychic discomfort and for these problems to be perpetuated long after the provoking conflict has past. These symptoms are, in a real sense, relics of by-gone days which are retained as disconcerting memorials to obsolete emotional struggles. They are preserved through the mechanism of psychological fixation and revivified through regression.

There is a system of logic in the inner emotional life which is quite distinct from the system of logic of the intellect. That is the first thing one has to understand about these psychological defense mechanisms. The individual has been driven back from the high aim of meeting life with the logic of intelligence, to dealing with it on a more primitive basis with the logic of the emotions.

With the above principles in mind, we will now discuss how they are applied. The initial phase is the *psychological evaluation*. This exploratory phase is best described as a process rather than a specific period in treatment —an ongoing process which is integrated into the total therapeutic regime. It can be described also by the shifts of intention of the examiner as the evaluation procedes rather than by a discussion of specific interviewing

techniques. The various aspects of the evaluation blend into each other with later phases evolving from preceding phases.

The first evaluation interview is approached with the intention of establishing a psychological frame of mind in the patient. The emotional factors have usually been disassociated from the somatic factors either by the patient himself, by the previous physician, or both. The vital importance of this psychological emphasis must be stressed. Often this is the single, most effective step toward improvement. A door can be opened and the patient can be seen as a person, not just as a collection of symptoms. Of course, this can be a threatening gesture especially if the patient is forced into a defensive posture as if accused of emotionality by the physician. An elaboration of this intent is the gentle insistence that the patient view his symptoms as an aspect of himself, not as a discomfort imposed from outside. He must see that he is an active agent in the initiation and/or perpetuation of the distress, not a passive object which can only endure discomfort. Next and usually in the same interview, the patient's life field is explored taking as a starting point the time of onset of the disorder, or the time of the current most significant exacerbation of the illness. This spring-board leads to an analysis of how the illness fits into the patient's life and brings to mind such questions as what does the illness keep him from doing? What does he feel he could be if he did not have the illness? What activities or plans did the onset of the illness interrupt? What are his feelings concerning the attacks, et cetera? Summed up, we are asking in essence what use does the patient make of his illness and we are attempting to assess the positive value in the illness (this is distinct from secondary gratification which provides a modicum of compensation in any illness). A concomitant intention which the examiner keeps before him throughout the interviews is an awareness of psychological pathology and a continuing assessment of ego capacity. It is important to get some idea of how well adjusted the patient is psychologically, how well controlled he is in terms of dealing with his emotions and how stable he appears to be. It is essential to decide whether we have a neurotic, psychotic, psychopathic, or psycho-physiologic personality.

The difference between these various types of personality may be exemplified by the following:

A man whose business is not going very well and whose folks are wealthy but stingy, has the natural thought that if his father died, he would be better off. If he's normal, he may have the thought consciously. If he's neurotic he may not have the thought consciously, but may instead, develop fears about his father's health, at the same time finding that he is accidentally leaving objects around, over which his father might trip. If he's delinquent, he may kill his father. If he's psychotic, he will tell you that his father is dead and that the man to whom he has just been talking is not his father. If he has a psycho-physiologic personality and is allergic, he may have severe symptoms and blame his work and environment.

SUMMARY

When emotions exist which cannot be expressed by words, actions, or thoughts, they may find expression through some organ or organ system. The organ which speaks is most likely the one which is constitutionally predisposed or has in some other way become invested with feeling when environmental conditions were stressful.

The major adjustment the doctor using the psycho-physiologic approach needs to make, is to get the emotional life of the patient into a biological frame of reference along with the organic data. He has to become accustomed to considering significant emotional responses as being just as real and as pertinent to the clinical picture as an eosinophilia or a wheeze in the chest. The interpretation of the psychogenic mechanism to patients with psycho-physiologic components requires the same professional matter-of-factness, the same sympathetic interest and understanding with which any other medical advice is given.

Simultaneous allergic and psychotherapeutic management is possible. Some physicians do not have the time, the training or the inclination to treat the patient psychotherapeutically as well as allergically. Even in these cases, however, the patient's emotional relationship to the doctor can have a psychotherapeutic function. If the doctor continues to emphasize during visit after visit that he understands how emotional tension is keeping the patient upset and his allergies active, and if he points out that the immunologic and pharmacologic therapies also have their value, then the patient benefits emotionally from the relationship. Physicians who have had training in psychotherapy may go even further than this. While they continue their immunologic and pharmacologic therapies, they also discuss emotional problems with the patient.

By using the psycho-physiologic approach, one will touch the lives of very many people more constructively than one might otherwise have done. We not only help the patient who comes to us but all the members of his family and other people with whom he is connected.

REFERENCES

1. Rosenbaum, M.: Critique of teaching psychosomatic medicine. Psychosom Med, 21:332, 1959.
2. Teaching Psychotherapeutic Medicine. New York: The Commonwealth Fund. 1947.

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CREDIT TO THE MAN

In science the credit goes to the man who convinces the world, not to the man to whom the idea first occurs.—Sir William Osler (1849-1919).

Historical Document

1895

PAROXYSMAL SNEEZING

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THIS TITLE has been chosen in order to direct attention to a very common condition, without presupposing any theory for the causation or pathology of an association of symptoms, of which the chief and most distressing are paroxysms of sneezing, that in many cases occur daily and in some cases several times a day throughout the year.

Paroxysms of sneezing, associated with profuse watery discharge from the nose and eyes, swelling of the nasal mucous membrane and nasal obstruction, which may be transient, are described as reflex in character. Certain physiological reflex actions commonly occur as the result of the irritation of the healthy mucous membrane of the nose; these are sneezing, lachrymation and coughing. For example, mechanical irritation of the anterior portion of the septum and turbinated bones in a case where the reflexes are of normal intensity may produce sneezing, lachrymation and rhinorrhea. If we pass the probe back along the septum or turbinated bones, or if we touch the pharynx near the Eustachian tubes with the probe, the nature of the reflex is changed and the patient coughs instead of sneezing.

These symptoms, sneezing, rhinorrhea, and the like, are found in several so-called diseases of the nasal mucous membrane. When occurring at certain seasons of the year, as early summer and early autumn, this group of symptoms are familiarly known as rose cold and hay-fever, and the pollen from the rose and certain grasses are supposed to be the exciting causes of the condition. There is another class of these cases, in which the attacks of sneezing do not limit themselves to any season of the year. In these the condition persists throughout the year, the attacks of sneezing coming on, perhaps, every day. These cases are named sneezing catarrh, false hay-fever, or other similar names. Cases of this last class are of such frequent occurrence that I wish to make a few general remarks concerning their symptoms, the local conditions in the nose associated with them, their relation to hay-fever and asthma, and the treatment which I have found most beneficial.

These patients present themselves with an account of their condition much as follows: they state that they have suffered from attacks of sneezing for

Reprinted from the *Buffalo Medical Journal*, August, 1895.
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years, occurring at intervals all the year round, are worse during the winter, or, perhaps the summer; on getting out of bed in the morning, or at any time during the night, the patient is immediately attacked by a violent paroxysm of sneezing, which may last for two or three hours. Dust, smoke or the atmosphere of a close room, a warm theater or concert hall, is certain to bring on an attack which compels the patient to leave the room or be very much embarrassed by a fit of sneezing. Fatigue or worry may, in these cases, bring on an attack, and the discharge from the nose and eyes is profuse and like water. These attacks are accompanied by tickling of the whole of the anterior of the nose, sometimes reaching into the fauces. During the attack, the patient complains of oppression of the chest; there may be a history of asthma in the family; a strong mental impression will often arrest an attack. After this condition has persisted for years, the patient may be awakened in the night with an asthmatic paroxysm, accompanied by coughing, which will probably occur night after night at the same hour. After this state of affairs has lasted for some time, the patient becomes irritable and nervous, complains of frontal headache and has a wornout, haggard look, produced by the constant mouth-breathing and want of sleep.

A rhinoscopic examination of several of these cases will not reveal a similar condition in each. In some there is but little apparent change of the mucous membrane; in others there may be excessive hypertrophy of the tissue over the lower turbinated bones, or of that over both the lower and middle turbinated bones, or there may be nasal polypi. There will, probably, be more or less deviations of and outgrowths from the nasal septum. The mucous membrane over the turbinated bones and the nasal septum in many, as well as in cases of true hay-fever, has a peculiar ashen gray color, is wet with the exuding serum, and has a soggy appearance, as if soaked in water. In others the mucous membrane is of a dark red color, but is bathed in the same watery secretions as the first class. Mulhall, of St. Louis, has compared these two conditions to the vasomotor disturbance seen in rage, one man's face being white while another's is livid. On examining the nasal mucous membrane with a probe, sensitive spots are found on the septum and turbinated bones, the touching of which produce violent attacks of sneezing. These spots are identical in character with those described by Sajous and J. N. Mackenzie as occurring in hay-fever. This, we can easily understand, is simply an exaggeration of the normal nasal reflex of the anterior part of the nose described above. The cough reflex is often likewise exaggerated when we have paroxysms of coughing at night accompanied by asthmatic breathing.

A person who has not passed through an experience of this kind cannot appreciate how mortifying it is to be compelled to sneezing perhaps every morning for years, to feel that an attack may come on at any moment and always at times when it will most embarrass and mortify the sufferer; for example, in the theater, during a call or at the dinner table. Some patients

are often compelled to use a handkerchief constantly for hours daily, especially in the morning, to receive the flow of serum and mucus. The hay-fever patient is fortunate compared with the individual suffering from the more chronic disease, for his trouble lasts but a few weeks, while hay-fever resorts are abundant and easily reached; but the poor sneezer must go on suffering the year 'round, unless treatment affords him relief. I have met with sneezing catarrh more frequently than hay-fever, my attention being first directed to this disorder because I suffered from it myself. I shall not attempt, at present, to report any of the cases of this condition which have come under my notice, but will call attention to certain points in them which illustrate their relation to hay-fever and asthma.

Although there are many of these cases in which the patients are not affected by the pollen of the plants which excite hay-fever and rose cold, nevertheless there are others that are much worse during the hay-fever season; while, on the other hand, many patients who have suffered from hay-fever for years, begin after a time to suffer from a similar condition all the year 'round identical in character with the condition which I have described.

Likewise, many cases of bronchial asthma are accompanied by paroxysmal sneezing, and many of those suffering from paroxysmal sneezing, after years, develop bronchial asthma, like their brethren with hay-fever. Ringer recognized, years ago, the intimate relation of these three—paroxysmal sneezing, hay-fever and asthma. He gives an exhaustive description of these conditions in earlier editions of his work on therapeutics, and illustrates their intimate relation to each other by the citation of cases.

It is evident from the clinical history of cases of hay-fever, rose cold and sneezing catarrh that they are identical in character, only differing in the exciting cause which brings on an attack and in their duration. Hay-fever and rose cold are excited by the pollen of certain flowers and plants and, consequently, only occur when the pollen of these flowers and plants are found in the atmosphere. In the other cases the attacks are brought on by a variety of causes, such as contact of the feet with a cold floor in the morning, the atmosphere of a warm room, and the like; and as such causes are always present when the local conditions of the mucous membrane are susceptible to irritation, they are likely to continue throughout the year unless successfully treated.

I do not wish, in this paper, to describe the pathology of these conditions, but if we accept the theory that asthma and hay-fever are due to a vaso-motor disturbance, and call hay-fever rhinitis vaso-motorea periodica, we must give to this condition the name rhinitis vaso-motorea chronica, and so on. Whatever theory is offered, the one must be accepted if the other is.

The same distinction is found here as between hay-asthma and bronchial asthma due to other causes. I should, however, prefer the name coryza vaso-motorea to rhinitis vaso-motorea, because there is really, in these cases, no inflammation, which is essentially a part of the disease and, if present,

is only accidental. The cases which have just been described must not be confounded with that condition which has been called nasal rhinorrhea, in which there is a constant and profuse running of serum from the nose, perhaps for hours daily. Several of these cases, by different authors, have been cited by Bosworth in his book. I have met this condition but twice in my experience. I am inclined to believe that the constitutional symptoms are due to the local trouble, i.e., mouth-breathing and want of sleep from nasal obstruction, but not so much to a neurotic habit or gouty orlithemic diathesis, although I believe that diet and exercise will do much to hasten a cure. The neurotic habit and psychial condition has probably much more to do with the production of true hay-fever than with causing paroxysmal sneezing, although the mucous membrane itself is more susceptible to external influences in these cases.

TREATMENT

The special diseased conditions of the nasal mucous membrane which predispose to paroxysms of sneezing, as has already been stated, are the same as those which predispose to hay-fever and rose cold, the chief of which are hypertrophic rhinitis, deflections and outgrowths of the nasal septum and nasal polypi, or any other obstructive conditions of the nose, which tend to produce chronic turgescence of the blood vessels of the mucous membrane. Therefore, special indications for treatment are found by a careful investigation and diagnosis of each case. Whatever lesion is found should be treated in the same manner in which it would be treated were there no such trouble present as the paroxysmal sneezing. Hyperthrophies, deflections of the septum and nasal polypi should be removed by the most approved surgical methods. In most of these cases there is, in addition to the gross lesions or, perhaps, without the gross lesions, the hypersensitive spots on the mucous membrane described above. These, of course, require additional treatment before the unpleasant symptoms, for which the patient has consulted you, disappear. I treat these, when on the turbinated bones and on the septum—and they occur most frequently on the septum—by touching them with pure carbolic acid, or with a solution of chromic acid in water of a 4 per cent to 10 per cent strength. This should, of course, be repeated until all the sensitive spots are made out and cauterized. This method of touching the spots I should prefer to the use of the galvanocautery, for I do not think that it is possible to use the cautery to any extent without producing a cicatrix. It seems to me all that is needful is counter-irritation, which is produced by the use of the acids of which I speak. This treatment, of course, should be supplemented, in most cases, by constitutional measures. I generally administer drop doses of Fowler's solution after meals, for small doses of arsenic seem to act well in controlling the sneezing; at the same time I advise light exercise in the open air and sunlight. The patient should avoid stimulating diet and the use of tobacco, especially cigarettes.

As soon as all pathological conditions of the nasal mucous membrane have been removed, and all sensitive areas producing either sneezing or coughing

have been carefully and thoroughly cauterized, the reflex manifestations disappear perhaps only for a time, yet often permanently. Should they return, it will only be in a modified and mild form, when the spots which have been overlooked at the first treatment should be sought out and cauterized. Perserverance in this sort of treatment will practically cure most cases and relieve all. This is the same treatment which I follow locally in the treatment of hay fever. I have been led to conclude, from cases that I have seen, that hay-fever, rose cold and sneezing catarrh are identical, the only difference being in the exciting cause of the paroxysm. The reasons which have led me to reach this conclusion are that the character of the attacks are the same, the appearance of the mucous membrane and the associated pathological conditions identical, while the same forms of treatment are the most beneficial in the majority of cases.

We must not, however, forget that in all cases of chronic nasal catarrh the nose is susceptible to the slightest irritation. These patients are said to be always taking cold; this cold taking varies in frequency with the amount of pathological change in the nasal mucous membrane. These attacks of cold in the head are often a passing paroxysm of sneezing; it seems to me that the difference between these cases and those of the classes of which I have spoken is more one of degree than of character. In many cases, whether of hay-fever, rose cold or sneezing catarrh, psychial influence seems to have considerable to do with precipitating an attack. An attack of hay-fever, for instance, which should have come on according to the patient's reckoning on August 20, at 4 p.m., can be delayed a couple of hours by turning back the clock that much. J. N. Mackenzie produced an attack of rose cold in a susceptible lady by suddenly producing an artificial rose in front of her. Dread of an attack of sneezing has often brought such an attack about in cases of sneezing catarrh.

OBSERVATION ON THE HISTORY AND CURE OF THE ASTHMA

Among the various chronic complaints for which the human frame is liable, very few can be considered of a more formidable nature than a confirmed asthma. The idea of its being an incurable disorder, its threatened instant suffocation at every attack, are circumstances altogether so alarming to a patient, as must necessarily weaken and depress the mind endowed with the utmost fortitude and resignation. Any remedy, then, that could be found capable of administering permanent relief, to the person in such an afflicting situation, must be looked upon as of the utmost importance in mankind.—MICHAEL RYAN, M.D., "Observation on the History and Cure of the Asthma," G. G. J. and J. Robinson, Paternoster-Row, London, 1793.

Progress in Allergy

HUMAN ECOLOGY AND SUSCEPTIBILITY TO THE CHEMICAL ENVIRONMENT

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(Conclusion)

Part VI. Treatment

Treatment of the manifestations of chemical susceptibility with synthetic chemical drugs usually is contraindicated, since these materials tend to *increase the burden* to which such persons are attempting adaptation. Not only may susceptibility spread to such man-made foreign substances but the body seems to resent maintenance-dose medications aimed at limited mechanisms. As a result of these so-called anti-drug responses, physicians attempting to treat the *effects of illness* frequently find that they are also treating the effects of past and present drug therapy.

As long as chronic symptoms are perpetuated by frequent or continuous chemical exposures to which susceptibility exists, a more fundamentally sound basis of therapy is needed. In the writer's experience, the following program, designed to *reduce* rather than *increase* chemical exposures, has been most helpful.

1. Chemical and other environmental excitants capable of inducing susceptibility and perpetuating chronic syndromes are suspected on the basis of probability and details of the history.

2. Suspected exposures are eliminated *concurrently*. This tends to induce non-adapted responses in which later re-exposures are apt to precipitate acute immediate reactions of diagnostic significance.

3. Materials so incriminated are then eliminated, if possible. Although such a program is detailed and restrictive, it remains the most workable long-term approach to the clinical problem presented by a chemically susceptible person.

4. Certain additional therapeutic measures in accordance with the apparent acid-hypoxia-endocrine-enzymatic mechanism of these responses,[44-47] are also helpful.

Descriptive differences between chronic effects from maintenance doses and acute symptoms following isolated exposures to the same material suggests the operation of somewhat different mechanisms. Although the

identity of these processes is not known, empirically, they seem to respond to different types of treatment.

A. THERAPY OF ACUTE REACTIONS

The basic principles in the treatment of acute reactions center about therapy aimed both at apparent mechanisms and the rapid elimination of excitants. These measures are most effective if instituted immediately and carried out conjointly.

Ingested Chemicals

Acute reactions resulting from the ingestion of chemical additives and contaminants of foods, biological drugs and water supplies, or chemical drugs are treated by emptying the gastrointestinal tract as soon as possible. Although this sometimes occurs as a result of the excitant itself, one is not justified in waiting for such a spontaneous effect. It may not occur; it may be considerably delayed, or the total effect on motility of the gastrointestinal tract may be characterized by constipation.

Although the alimentary canal may be emptied by means of various laxatives and enemas, the writer prefers the oral administration of the bicarbonates of sodium and potassium because of their *multiple effects.* This mixture not only exerts a laxative action but also combats the apparent acidity involved[44,45] and, if employed in the correct proportions for given individuals, seems to have a diuretic effect. Finally, it may also exert a mode of action apparently not dissimilar to that of ACTH and related materials.[47]

Alkali salts are administered as soon as possible after cause and effect relationships of acute reactions have been demonstrated. This is accomplished by giving between 10 and 15 gm of mixed alkali (usually ⅔ sodium bicarbonate and ⅓ potassium bicarbonate) in approximately a quart of *spring water.* The use of spring water is stipulated because the dose of chemical contaminants in the amount of tap water required may induce an acute reaction, especially if generally available water supplies had been avoided. In the event a laxative effect has not occurred within two hours, an additional 5-7 gm of mixed alkali salts similarly diluted, or a spring water enema, is given.

There are certain individual differences apparently involved which, for optimum effects, may require variations in the proportions of sodium and potassium bicarbonate: the occurrence of fluid retention, as manifested by puffy eyes or other evidence of edema, or, if one is interested in a more prompt laxative action, increasing the proportion of potassium bicarbonate up to 50 per cent may be helpful. Occasionally, where it has been necessary to treat successive acute reactions in this manner, it is desirable to use magnesium oxide in the form of milk of magnesia either supplementally or intermittently for its laxative action.

In instances of severe nausea and vomiting, the alkali combination may be administered by enema, or sodium bicarbonate may be given intravenously.[45] The recommended dosage is 7.5 to 10.75 gm (two to three 50.0 cc ampules) of a 7.5 per cent solution.** This may be introduced either by an intravenous drip or by means of a 50 cc syringe. There seems to be no contraindication to injecting the material as rapidly as may be delivered by a 21 gauge needle. Leaving the delivery needle *in situ* and filling the syringe by means of a larger needle facilitates the administration.

The injection is continued until acute symptoms subside; until the onset of an excessive thirst, or until the full amount has been given. If such a dose is ineffective in the treatment of an acute reaction, larger amounts usually are not helpful. Immediately prior to the onset of an excessive thirst, the patient may notice gastrointestinal rumbling or tingling of the lips or face. Occasionally, transient chilling may occur either during or immediately following an injection.

Either oral or intravenous alkali therapy—especially the latter—is contraindicated in instances of *cardiac or renal failure and during pregnancy.* The general safety of sodium bicarbonate intravenously has been attested by detailed observations.[48]

Other Acute Reactions.—Acute reactions from *inhaled, injected,* or *contacted chemicals* may also be treated effectively with similar doses of alkali salts. It should be emphasized that this therapy is effective in the absence of diarrhea, although the laxative action may be additionally effective in aiding the elimination of retained fluids. As in the therapy of acute reactions resulting from ingestants, the earlier alkali treatment is started, the better.

Oxygen

Inhalation of oxygen by metal nasal catheter and Tygon tubing is effective early in the course of acute reactions from inhaled chemical exposures. The use of this special *non-odorous plastic tubing* and avoidance of *odorous rubber tubing,* masks, breathing bags and plastic tents is advisable in view of the tendency of odorous rubber and plastic to induce or perpetuate symptoms. Although oxygen may also be helpful in the therapy of acute reactions from ingested chemicals, it does not ordinarily substitute for alkali treatment.

Patients with high degrees of susceptibility to chemical exposures profit by having a small tank of oxygen in their homes for emergency use. Some find that carrying an emergency oxygen case is useful in traveling.

Drugs

A limited number of biological drugs are helpful in the treatment of acute reactions. These include such natural sypatheticomimetic prepara-

**Manufactured by Abbott Laboratories, North Chicago, Illinois.

tions as ephedrine and epinephrine. *Natural* antibiotics are preferable to synthetic ones. Codeine and other opiates are preferred over synthetic analgesics. Antihistaminic agents, barbiturates and other synthetically derived drugs may be helpful when used occasionally, but are preferably *avoided.*

Specific susceptibility to biologic drugs or their chemical additives and contaminants may occur, as previously described. When drug therapy is mandatory, there are times when a synthetically derived drug may be less objectionable than a biologic product to which a given individual is sensitive. But when acute reactions are adequately treated with alkalis and/or oxygen, additional drug therapy—including that with corticosteroid hormones—is usually not necessary.

B. THERAPY OF CHRONIC REACTIONS

Avoidance of Incriminated Offenders

The *avoidance* of incriminated excitants to which a person has been found susceptible remains the *treatment* of choice. Specific details of how this is accomplished has been touched upon earlier and will be summarized later. Although such a regimen may be highly restrictive, no equally satisfactory program is available. It is also admitted that such avoidance programs often entail considerable expense and inconvenience, especially if indoor air pollutants and chemical additives and contaminants of the food and water supplies are involved. However, if one is sufficiently sick and disabled and especially if other means of control have been exhausted —as so often is the case—such an avoidance program is readily accepted. Furthermore, the demonstration of the *causes* of illness comes as a welcome relief to many chronically sick persons.

Alkalis and Oxygen

Alkali therapy is not recommended for the treatment of chronic reactions of the type previously described and resulting from susceptibility to and exposure to chemical and other excitants. Although a maintenance dose of sodium and potassium bicarbonate may assist in the treatment of relatively minor chronic symptoms, it is usually insufficient to relieve major symptom syndromes and sometimes actually accentuates them. The writer has had the unfortunate experience of inducing sharp accentuations of status asthmaticus, protracted migraine headaches, chronic depressions, and certain other advanced *chronic* manifestations following intravenous alkali therapy.

On the other hand, certain specifically diagnosed patients may find that restrictions do not need to be quite as exacting when taking a maintenance dose of alkali salts. For instance, a correctly diagnosed patient, aged eighty-three, subject to chronic arthritis, headaches and depression when eating regularly of specific foods and especially chemical additives and contaminants of food and water, remains relatively symptom-free when avoiding exposures to which susceptibility has been demonstrated. Never-

theless, she claims to *feel better* when taking a daily dose of five grams of mixed alkali salts each morning—a program she has continued for the past decade. Each of several times that her electrolytes have been checked, normal values have been found. Although alkali therapy may be used effectively as an adjunct to an *avoidance program,* this usually is not necessary.

Oxygen therapy is of only limited value in treating chronic reactions but, as with alkali therapy, is very helpful in tiding over acute exacerbations of chronic syndromes. Again, the quicker either is instituted, the more effective.

Drugs

Patients already susceptible to certain facets of the chemical environment are known for their ability to develop *new* susceptibilities to *other* chemical and biologic exposures to which they are frequently subjected. Maintenance doses of drugs are particularly effective in inducing such chronic syndromes. Since maintenance *drug dosage* tends to add to the patient's load of materials to which he is attempting adaptation, they are generally contraindicated. A spread of susceptibility to such chemically derived drugs is to be expected. Not infrequently patients give the history of having had to discard one such preparation after another.

Corticosteroid hormones are not recommended in the treatment of chronic reactions, although ACTH seems to be less troublesome than the others. They may be temporarily effective; however, such programs are not only expensive but frequently result in troublesome complications. One of the most troublesome features of corticosteroid therapy is the tendency for symptoms to be accentuated immediately after these drugs are stopped.[49] But even more important, the patient previously treated with corticosteroid hormones seems to be much more difficult to diagnose and treat specifically thereafter. Although the complications of prolonged corticosteroid therapy may be less troublesome than at first suspected, these preparations do *not* provide satisfactory answers to long-term chronic illness.

Specific Injection Therapy

Certain chemically susceptible patients, also sensitive to house dust, have obtained considerable relief of chronic symptoms as a result of receiving regular injections of *house dust extract,* although preservative-free materials may be required. A similar mutual relationship between chemical susceptibility and pollen, mold, and food sensitivity has also been observed. Despite the helpfulness of such a specifically oriented injection schedule, it does not ordinarily provide completely satisfactory relief of symptoms. Unfortunately, it has the additional disadvantage of adding to the load of materials to which a chronically sick person is attempting adaptation. This interpretation apparently accounts for the necessity of *discontinuing all injection therapy* in certain instances.

It should be emphasized, however, that certain individuals with multiple susceptibilities do not require injection therapy with extracts of house dust, pollens, or spores *when avoiding* chemical and food exposures to which susceptibility has been demonstrated.

Two unusually interesting patients, both of whom are susceptible to house dust and chemical excitants, obtain a period of relief of their chronic symptoms only as a result of house dust injections *containing phenol* as a preservative. This has been demonstrated repeatedly by employing phenol-containing and phenol-free extracts blindly. Both persons identified the beneficial effects produced by the preservative containing injections as against a nil effect of the same dose of phenol-free house dust extract. The possibility of this being an adapted response to the phenol cannot be excluded, but injections of the phenol-containing diluent only were less effective than when combined with the usual dose of house dust.

General Measures

Control of infectious processes, especially amoebiasis and other chronic parasitic and microbial infections is helpful, since invading microorganisms and inaminate excitants apparently impinge on common defenses—including the ability to develop immunologically protective responses. Similarly, the control of thyroid and other endocrine deficiencies should not be neglected.

A program of regular active physical exercise or other measures to increase and maintain muscular tone and circulation are sufficiently beneficial to be all that may be required to counteract low grade chronic reactions.

Avoidance of *excessive* physical fatigue may also be of assistance but, more commonly, fatigue, irritability, and the tendency for inter-personal and emotional responses are more readily demonstrable as *effects* rather than additional *causes* of illness in the persons studied.[17]

C. PROPHYLAXIS

Specifically Diagnosed Cases

As previously stated, the patient already susceptible to certain excitants tends to develop a *spread* of the process to other facets of the chemical environment to which chronic exposures are maintained. Conversely, when diagnosed patients *avoid* as many chemical exposures as possible, the process is far less apt to spread. Furthermore, such a program usually is associated with a decreasing degree of susceptibility to incriminated chemical excitants. This course of events was illustrated in the second case report, in which chemical exposures that formerly induced *acute* depressions subsequently precipitated only episodes of rhinitis and coughing.

But once a high degree of susceptibilty to a chemical excitant has developed, even though it may be *reduced as a result of avoidance,* it may

be reactivated quickly by later chronic exposures. Intermittent exposures may do likewise.

Specifically Undiagnosed Cases

Although the *scope* of the chemical environment precludes its avoidance prophylactically, there are specific exposures about which we, as a race, have been extraordinarily careless. Among these chronic exposures are *indoor* chemical air pollutants arising from gas utilities and other indoor hydrocarbons. Equally troublesome is the indiscriminate practice of spraying foodstuffs with insecticide-solvent mixtures. The potential dangers of these daily chemical exposures—insofar as the general health of all is concerned — is such as to warrant a far greater degree of protection, prophylactically, than presently exists.

The magnitude of the clinical problem associated with indoor hydrocarbon exposures and outdoor traffic exhausts underscores the urgent need of improvements in the design and combustion efficiency of gas kitchen ranges, heating systems and automobiles.

The downhill clinical course of many patients is also associated with the indiscriminate use of chemical drugs. Both the general public and the medical profession need to be alerted to the potentially hazardous effect of over-zealous drug therapy. It is well to recall that a physician's *first responsibility* to his patient is *not to harm him.* This responsibility is rapidly becoming more hazardous, in view of the *increasing susceptibility of patients* to chemical excitants, on the one hand, and to the progressive monopolization of medical supplies by chemically derived drugs on the other. Indeed, this hazard is so great—insofar as certain patients are concerned—that there is no satisfactory alternative to that of determining what parts of the chemical environment may already be involved and helping the patient to *avoid* those exposures.

Part VII. Case Reports

Earlier case reports were selected to illustrate the development and scope of the clinical problem presented by the *chemically susceptible patient.* The following reports illustrate the applicability of the program of comprehensive environmental control and subsequent re-exposures as diagnostico-therapeutic measures.

S. D., a surgeon, forty-two-years-old, was seen because of a progressive agitation-depression syndrome that had failed to respond satisfactorily to psychiatric management.

Following eczema in infancy, he had continued to have a dry, easily irritated skin. Acute rheumatic fever was diagnosed at twelve years, because of the occurrence of fever, painful joints, fatigue and irritability. This was treated with large doses of acetylsalicylic acid until the onset, after a few weeks, of generalized urticaria and bronchial asthma. Both manifestations subsided after this analgesic was discontinued.

The rare occurrence of hives in recent years—usually occurring after eating seafood—had been treated by means of antihistaminic drugs. During the year prior to his initial visit in 1959, he had been subject to increasingly severe generalized edema. Asthma never recurred.

In 1949 he was diagnosed on x-ray evidence as having a peptic ulcer, which healed satisfactorily on medical management. His only gastrointestinal manifestations in recent years have been vomiting and/or diarrhea following seafood.

Phenergan was first taken in intermittent doses for the relief of acute rhinitis, but more recently has been used in nightly subcutaneous doses of 25-50 mg.

Headaches, which had been present for a decade and increasingly constant for the past year, were known to have been accentuated by exposure to traffic exhausts, the odor of solvents, fresh paint, and certain other volatile hydrocarbons. Largely because of the headaches resulting from traffic odors, he moved from a metropolitan area to a small town in 1953.

Chronic fatigue had also been a major complaint since age twenty. The degree of tiredness was unrelated to the amount of work done or rest obtained. Although it was worse certain days, for no apparent reason, chronic fatigue was present to some extent *every day* and came to be associated with an increasing level of generalized muscle fatigue and aching.

Becoming extremely hyperactive after using opiates, he often used meperidine for the relief of headaches. Daily injections for the control of pain had also been received during three traumatic episodes in the year prior to his first visit. He gradually drifted into taking daily injections, regularly, of Phenergan and Demerol; otherwise, he remained extremely nervous and jittery. Isolated injections of local anesthetics also increased his nervousness.

Insomnia became increasingly troublesome. Chronic fatigue, profuse perspiration, nervousness, irritability, and a progressively troublesome tremor materially interfered with his work. Sexual maladjustment and other abnormalities of behavior developed, with a progressive tendency for hyperactivity and agitation to alternate with gradually increasing episodes of fatigue, headache and depression.

This patient was hospitalized for specific diagnosis and treatment at a time when the history of apparent addiction to meperidine was not known. On the second day of fasting and the avoidance of all drugs, tobacco and other exposures previously described, he became increasingly restless, nervous, depressed and achy. All symptoms were accentuated on the third day when he developed a temperature to 102.5 degrees F. Residual myalgia, fatigue and rhinitis tapered off the fourth day.

At this point, when relatively symptom-free, he threw a window wide open—against strict orders—and air heavily polluted by refinery odors was carried in by a southeast drift wind. Soon, he began to complain of feeling flighty, jittery and tense; claimed to be unable to read comprehendingly, and seemed to be preoccupied with one-track thoughts. Insomnia and restlessness, characteristic of the early part of this attack, were followed by residual fatigue and nasal stuffiness.

After recovering from this reaction and on the seventh day of the fasting program, single foods of known cultural pedigree were returned to his diet. After several foods had been taken without incident, he reacted to potatoes boiled in spring water. His resting pulse prior to this feeding was 72; his pulse rates at twenty-minute intervals following were 84, 96, and 72. Distension and gaseous eructations occurred immediately. A severe headache developed at two hours and was followed shortly by vomiting. Restlessness and insomnia characterized the first few hours of this reaction; depression persisted through the night. Despite emptying the gastrointestinal tract by means of alkali salts and milk of magnesia, a weight gain of two pounds was noted the following morning. He then gave the additional history of commonly vomiting after "eating out," at which time he usually ate a ***baked potato***.

Although natural (chemically uncontaminated) corn failed to react, commercially

available *corn meal* and *corn sugar* were followed by immediate abdominal distress and gaseousness. Projectile vomiting occurred two hours later. He remained awake throughout the night, becoming extremely depressed toward morning, at which time he threatened to leave the hospital.

The first time commercially available eggs were tried, tachycardia (72:78, 94 and 78), insomnia and irritability were the only developments. He was subsequently fed eggs of known cultural pedigree, from the same source as those tolerated by other chemically susceptible patients. Increased salivation occurred immediately. A headache developed at two hours; vomiting followed. Despite a profuse diarrhea after taking alkali salts and milk of magnesia, his headache persisted and became associated with nervousness, apprehension, wringing of hands and a subsequent depression. He finally fell asleep at 4 a. m. Upon awakening at 6 a. m., he was symptom-free.

After not having reacted to *other foods* used regularly in his diet, he was checked for susceptibility to chemical contamination of the diet by means of several meals of previously *unsuspected uncommon foods* known for their chemical contamination. Nothing was observed after a breakfast of commercially available canned blueberries sweetened with Sucaryl, nor a lunch of canned tuna, canned dietetic cherries, frozen cauliflower and raw apple. Two hours after a dinner of canned salmon, canned dietetic peaches, frozen broccoli and raw celery, he noticed the recurrence of nervousness, tremor, jitteriness and hyperactivity. Insomnia persisted until 4 a.m., at which time he finally fell asleep, the phase of hyperactivity being followed by depression. Since natural—chemically uncontaminated—sources of these foods have since been tolerated, this response may be interpreted as the *cumulative effect of chemical additives and contaminants* of these foods.

At a time when symptom-free, he was discharged home on a test-compatible diet, spring water, and without drugs. During the first two days there was no immediate effect when he remained in his electrically equipped home in the summertime. He also returned to drinking local well water without reaction. However, each time his wife wore *hair spray* a typical recurrence of insomnia developed. Upon two different occasions, exposure to *fresh paint odors* at the hospital was followed by a recurrence of tremor, hyperactivity, irritability, a delayed depression, ankle edema, and a weight gain of nine pounds. Several lesser grade exposures followed breaks in the diet before a consistent chemically uncontaminated source of foods was worked out. Eggs and potato still caused severe reactions, even though *not* chemically contaminated.

He has remained symptom-free and without drugs for the past several months while following a chemically uncontaminated diet, avoiding eggs and potato. His weight now remains constant instead of fluctuating widely. He is able to work long hours without tremor and with far less fatigue than formerly, although prolonged exposure to certain anesthetic odors in the operating room are slightly troublesome. Profuse perspiration—formerly a major handicap when operating—is no longer present. Sexual adjustment is now satisfactory. He is apparently a happier and more pleasant person, insofar as his family and associates are concerned, and he is *far more productive* in his work.

Since this patient did not have a major susceptibility to *home installations,* the reaction of two *other* patients upon returning home will be cited briefly to illustrate these factors.

M. W., a forty-two-year-old housewife, subject to rhinitis since infancy and, more recently, chronic fatigue, headache and intermittent periods of depression, became symptom-free in the hospital. She was discharged on a compatible diet and water supply and without drugs.

There was no obvious reaction during the first 36 hours at home, during which time the gas kitchen stove was used only minimally. The afternoon of the second day home she used the gas kitchen stove in baking for a period of three hours. Within the first hour she had a recurrence of nasal stuffiness, followed by profuse rhinorrhea. She then became increasingly irritable and subsequently depressed. When the gas range was moved to the garage, she felt generally better. Symptoms recurred when it was *returned* to the house and used, irrespective of the type of food cooked.

Since the permanent removal of the gas range and the continued avoidance of major contaminated foods, she has remained relatively symptom-free except for occasional accidental exposures. These usually have followed visits in *other homes* or attempts to eat in poorly ventilated restaurants in which gas kitchen ranges were used.

N. R., housewife, age thirty-one, was first seen because of repeated bouts of rhinitis, fatigue, headache, myalgia, and low-grade temperature elevations suggestive of influenza. She also complained of being dopey, groggy, unable to read comprehendingly or to think clearly. When these symptoms were intensified, she usually was depressed. At other times she was irritable, unsteady on her feet, and frequently dropped things.

She was found highly sensitive to several common foods. Although she profited by their avoidance, she remained chronically sick. The fact that she was better during summer months and on vacations when away from home; also the fact that her symptoms *recurred soon after she returned home* suggested susceptibility to house dust or indoor chemical air pollution. Although she was found skin-test-sensitive to house dust and knew that dust exposure accentuated her rhinitis, treatment at various levels with house dust extract did not afford satisfactory relief.

Her chronic symptoms during winter months were at least 50 per cent improved following the *simultaneous elimination* of her gas range, gas refrigerator and gas water heater from her kitchen and the *substitution of electrical equipment.*

Feeling relatively better most of the time after this change, she then was able to detect the effects of *other* previously unsuspected chemical exposures. One by one, acute reactions were traced to her husband's use of after-shaving lotion, spray deodorants in the bathroom, the inhalation of the odors of synthetic alcohol and synthetic vitamin preparations, the use of weed-killing sprays on the lawn, the odors of the municipal mosquito abatement spraying, odors from tarring of roofs and roads, wearing an Orlon sweater, traffic exhausts, and many others.

But despite following a restricted diet—including a chemically less contaminated food intake—she still remained inexplicably ill most of the winter months. When alternating depression and irritability-nervousness, dizziness and panic recurred in the fall of 1955, the family decided to follow through with the previous recommendation to replace their warm air furnace with hot water central heating, installing the furnace in the garage.

With the control of indoor air pollution, the avoidance of major chemically contaminated foods, and certain other specific substances, this patient has remained well. From time to time, additional chemical exposures have been detected—one of which was the odor of a colored plastic telephone. With the mother's improved health, an important and unexpected development has occurred: the better health and behavior of the grade school children in this family. They are happier, less quarrelsome, and have greatly improved in their school work.

Part VIII. Instructions for Avoiding Chemical Additives, Contaminants and Drugs

The following brochure, to which local sources of chemically less contaminated foods may be appended, has been found helpful in the instruction of patients. However, it is *not* to be used for this purpose until *after* a patient has *answered his questionnaire,* as given in Part II.

Clinical susceptibility to gas, oil and coal—including their combustion products and related derivatives—is a common unsuspected cause of chronic illness.

The exposures to be described have been demonstrated as causative factors in the investigation of over a thousand patients susceptible to chemical additives and contaminants of air, food, water and biological drugs, as well as synthetic chemical drugs and related materials. Although no one is susceptible to *all* of these materials, a large portion of this chemical environment may be involved either by inhalation, ingestion, injection, or by contact. Once started, this process tends to increase in degree and to spread to related substances to which one is chronically exposed.

There are various stages of susceptibility to chemically contaminated air, food, water and biological drugs, synthetic drugs, cosmetics, textiles, rubber, plastics, and other chemically derived materials. When a slightly susceptible person is first adapting to oft-repeated or constant doses of one or more of these agents, he tends to remain energetic and relatively symptom-free. He may even express a liking or fondness for exposures acting in this manner.

But as adaptation to these everyday materials decreases, characteristic overlapping and cumulative effects develop so insidiously that victims rarely know their causes. When such a person is asked about a given substance, he might reply that he liked it; that it had no apparent effect; that he disliked it, or that it made him sick. His answer would depend upon his degree of susceptibility to it and to variations in the frequency and size of exposure. For instance, a person susceptible to various chemical exposures is more apt to suspect fresh paint odors (encountered only occasionally and in relatively concentrated amounts) than the odors arising from a gas kitchen range or warm air heating system (from which he is rarely separated for more than a few hours at a time).

Whether certain chemical exposures are suspected also depends on a person's sense of smell. Although many victims of this illness have an extremely *acute* ability to detect the odors of escaping gas and other chemical fumes—far beyond that of those non-afflicted—the reverse may also be true. Certain advanced cases having an impaired sense of smell are at an additional disadvantage in protecting themselves from exposure to various chemical odors and fumes.

Individuals affected adversely by chemical additives, contaminants and drugs are apt to be sensitive to pollens, spores, animal danders, dust, or

other biological materials which may cause identical symptoms. *Avoiding as many offenders as possible is indicated.*

INDOOR CHEMICAL AIR POLLUTION

Indoor chemical air pollution is primary; it must be brought under some degree of control before attempting to observe the clinical effects of *other* chemical exposures.

Homes.—Indoor chemical air pollution is especially difficult to detect because of the constancy of major contributing exposures, namely, the odors and fumes from gas kitchen ranges; gas or fuel-oil space heaters; gas refrigerators and other gas burning utilities; warm air furnaces, and odors of rubber, plastic, insecticides, perfumes, detergents, bleaches and cleansers. Although susceptibility to indoor chemical air contaminants characteristically produces winter illness, it may cause perennial or summer-accentuated symptoms. With open windows, relatively more volatile summer traffic odors, which are also produced by relatively more traffic than in winter, enter homes more readily. In the presence of closed windows, evaporation of filter oils in air conditioning equipment or the odors of electric fans or other motors may be troublesome. Fans—as integral parts of warm air, hot water or electric room-heating units—are not recommended.

Since susceptibility to chemicals usually accompanies clinical susceptibility to biological excitants, the simultaneous avoidance of *all* common exposures on the basis of probability is most apt to relieve a patient's chronic symptoms. This is best accomplished by fasting a patient in hospital quarters relatively free of odors and fumes as well as pollens, spores, danders and dusts. During this time the patient should avoid drugs, cosmetics, tobacco and synthetic textiles in wearing apparel, and should drink only spring water. The effects of returning single chemically uncontaminated common foods is first noted. Then the effect of returning chemically contaminated foodstuffs is observed. Incriminated materials are avoided as detected.

Then the symptom-free patient on a compatible intake of food and water is returned to his previously avoided home surroundings, working conditions, local water supplies and avocations. If a person worsens after returning home under these circumstances, susceptibility to indoor air pollutants is probable. The gas kitchen range or gas or fuel-oil space heaters are first to be suspected. The effect of removing these from the home, temporarily, and returning them is noted. It should be emphasized that merely turning off the gas line to the house does *not* constitute an adequate test, since seepage from unused gas utilities may perpetuate chronic symptoms. If incriminated, it is usually necessary to replace all gas utilities with electric equipment and it may be advisable to remove all gas pipes from the house.

Warm air furnaces are also common causes of winter symptoms but this usually is best checked after the above exposures have been appraised. Warm air furnaces sometimes leak between their combustion and warm air chambers or puff when turned on, emitting combustion products through cold air intakes, floors, walls, and up stairwells and laundry chutes. Many chemically susceptible patients seem to react to the first blast of warm air when such furnaces turn on automatically.

The type of furnace fuel which is used is relatively unimportant since each has disadvantages. Gas tends to leak at various joints in the line. Oil burning furnaces have a characteristic odor which is accentuated if the storage tank is located in the basement or if it has overflowed. Coal usually is soaked with kerosene when delivered; this slowly evaporates and fouls the air of the basement. Coal-fired furnaces sometimes burn into the spiral of the stoker, smoking the basement. Fireplaces burning coal are apt to puff; those burning pine wood may also emit troublesome odors. Downdrafts in an unused fireplace flue of a double chimney may carry fumes from an adjacent flue into living quarters.

Since there are major objections to both warm air furnaces and to fuels stored or burned in the house, *electric heating* or *hot water* or *steam central heating, with the furnace located in an adjacent garage or outbuilding,* is recommended. Neither the furnace room nor the garage should be located in the basement. Neither should either be entered directly from the house by means of an intercommunicating passage, in view of the ease with which odors and fumes may contaminate the living quarters.

Apartment dwellers should not live adjacent to or directly above the furnace room or garage, but even upper floors may be contaminated as a result of motor exhausts of basement garages entering elevator shafts. In general, those highly susceptible to chemical additives and contaminants are more comfortable living in *all-electric* apartment buildings rather than those containing both gas and electric utilities.

Toxic insecticides, such as dieldrin, chlordane and pentachlorophenol are often used by professional exterminators for control of termites and ants. Do not permit the use of these chemicals under your home or in your attic. Arsenic is much less toxic, when control is imperative. Rugs, rug pads and blankets are often moth-proofed by the use of DDT and other insecticides as purchased or in clearing or storage. Be careful to avoid such treatment.

The air of living quarters may also be fouled by the odors of sponge rubber pillows, rubber mattresses, foam upholstery, rubber rug pads, rubber or plastic backing of rugs and carpets or plastic upholstery, plastic folding doors, plastic telephones, plastic shoe bags and plastic bedding covers. Similarly, the use of perfume, cologne, scented soap and shampoo, nail polish, nail polish remover, cigarette lighters, lighter and cleaning fluids, household deodorants, disinfectants, Lysol, phenol, insecticide sprays, bleaches, cleansers containing bleach, and ammonia may not be tolerated.

Many react to the odors of moth balls or crystals; floor wax; furniture, shoe or metal polishes; fresh newspapers; tobacco smoke; Christmas trees and other indoor evergreen decorations; pine oil and pine-scented cleansers and toilet articles. The majority are highly susceptible to the fumes of turpentine, mineral spirits, synthetic alcohol and evaporating paints, varnishes, shellacs, lacquers, and various solvent and/or tar-containing adhesives. *Interior decorating and the laying of tile or flooring should be done in the patient's absence and be odorless before his return.* In general, *casein* or *alkyd based paints* are better tolerated than rubber based paints or those containing turpentine or mineral spirits.

Aerosol bombs or sprays containing lindane, methoxychlor, DDT, chlordane, malathione or thiocyanates should *never* be used indoors and only with great caution outdoors. For mosquitoes, moths, flies and other insect pests, "Aerosect" aerosol bomb (made by the Pennsylvania Engineering Company, Philadelphia 23, Pennsylvania), containing pyrethrum and rotenone in a base of sesame oil may be used with caution. "Ortho-extrax" spray with rotenone and pyrethrum, when mixed with water, is the least harmful spray for ant invasion. However, these contain petroleum oils and should be avoided indoors.

Leaking refrigerant gas may also cause acute or chronic symptoms. This is not only used in electric refrigerators, deep freezes and air conditioning equipment, but also is the compressed repellent in most dispensers of the bomb type for insecticides, perfumes, hair sprays, whipped topping and various other foods and drugs. Leaking refrigerant is suggested by a gradually decreasing refrigerator frosted coil surface or by *reactions* to stored or frozen food when the same lot of food had been tolerated *prior to* storage or freezing.

Public Places.—Many patients react to the contaminated air of bus or train depots or from riding in diesel buses or trucks. Some are troubled by contact with or the odors of pine-paneled interiors; mineral oil treatment of bedding, furniture or rugs to allay dust; deodorants used in theatres, public toilets or other public places; the odors of perfume and other highly scented cosmetics emanating from crowds; perfume counters of drug and specialty stores; rubber or plastic odors of new automobiles or chlorine odors from indoor swimming pools. Some students and teachers are made mentally sluggish by inhalation of the exhausts of gas stoves in the school's cafeteria, home economics rooms, or by odors arising from improper heating or air conditioning equipment. Some persons—when otherwise avoiding major exposures—may react sufficiently to the odors of gas ranges, other unvented gas utilities and warm air heating systems to preclude shopping or visiting in quarters so equipped.

OUTDOOR AIR POLLUTION

Metropolitan outdoor air contamination is most marked downtown and in industrial areas, being heaviest in the vicinities of refineries, gas works,

paint and chemical factories, rubber and sulfur processing plants, steel mills, fertilizer plants, et cetera. Those susceptible to chemical odors and fumes should try to live to the *windward side* of such metropolitan and industrial areas—as far away from them as possible. Since contamination extends peripherally along roads and railroads, such persons profit by living at least three blocks from expressways and railroads and avoiding areas of decelerating traffic, such as at bus stops and stop lights. Driving to the *windward side of* multi-laned traffic is helpful. Try to keep at least four car lengths behind other vehicles when stopping for lights or crossings. Avoid heavily traveled routes. Close your car windows and turn on inside air *only* when passing diesel trucks or buses, or when driving through excessively contaminated areas.

Ordinarily, one is less exposed to the fumes of his own vehicle when riding in the front seat and keeping rear and rear-side windows closed. Automobiles having defective exhaust or brake systems, improper carburetor adjustment, or using an excessive amount of oil, should be *repaired* or *discarded.*

Air pollution in metropolitan areas is accentuated at street level; in the basements of downtown streets; in subways; on quiet, humid or rainy days, or when the wind is blowing gently from the vicinity of refinery or industrial areas. *Visibility* is the best single *index* of *air pollution* in Chicago. Eye irritation may occur.

Air pollution is dispersed through residential areas in various ways—from traffic exhausts, home heating units, home incinerators, and spraying for insect control. Odors and fumes from burning of home refuse are highly irritating, due in part to the bulk of waxed food cartons in such dry garbage. Mosquito abatement programs or spraying lawns, gardens, orchards, farms or forests for the control of insects or weeds menaces the health of many highly susceptible persons. Such victims should request advance notification of such spraying by their neighbors or municipalities so as to be able to protect themselves or to flee from the area. Chemical air contamination, no longer limited to cities, is becoming a major problem in rural regions due to widespread spraying processes and the use of mechanized farm equipment.

Although pollens, spores and larger dust particles ordinarily are removed by the filters in air conditioning equipment, *chemical air contaminants are not removed.* In fact, chemical odors and fumes may be accentuated by evaporation of the filter oils in such equipment. Chemical fumes and cooking and smoking odors may be effectively removed only by *activated carbon filters,* provided such equipment contains a *sufficient quantity* of activated carbon for this purpose. However, such installations in warm air furnaces have not proved satisfactory. As an emergency measure, breathing through a gas mask cannister protects one from unexpected exposures such as might be encountered in driving over freshly tarred roads, through refinery areas, in the vicinity of spraying rigs or diesel

trucks or buses. An activated carbon civilian defense gas mask may be purchased from surplus military supply stores. Only the cannister is to be used, as the rubber of the mask may induce additional symptoms because of its odor.

DRUGS, COSMETICS AND PERSONAL CONTACTS

Drugs.—Certain biological drugs, especially those designed for injection —such as epinephrine, insulin, liver extract, allergen extracts, et cetera— usually contain phenol, chlorbutanol or other chemical preservatives capable of causing reactions in individuals highly susceptible to chemical additives.

Persons susceptible to chemicals and related materials should also avoid the use of such synthetic chemical drugs as aspirin (Anacin,® Bufferin,® Empirin,® Empirin Compound,® acetylsalicylic acid and certain cold remedies); sulfonamides; sulfur-containing preparations, barbiturates and most other sedatives; tranquilizers; antihistaminic drugs and many antibiotics. Mineral oil, petroleum jelly, vaseline or ointment bases of synthetic origin as well as preparations containing synthetic dyes, scents or preservatives may also cause trouble in these individuals. This usually means the avoidance of hand lotions, laxatives, most ointments and creams, tar and creosote-containing preparations and synthetic vitamins. The odor of or contact with synthetic alcohol and certain adhesive tapes may be troublesome. In general, *the patient should use only approved biological drugs* known by his physician to be free of chemical agents or contaminants and recommended by him. Even though a given synthetic drug may seem to be taken initially without difficulty, if one is already susceptible to many materials of synthetic origin, prolonged use of synthetic chemical drugs often is associated with a spread of susceptibility and an increasing medical problem insofar as susceptibility to the chemical environment is concerned.

Cosmetics. — Commercially available lipstick, nail polish, nail polish remover, perfume, cologne, scented soap and shampoo, detergent shampoo, cold cream, foundation cream, deodorants, after-shaving lotion, hair tonic, hair spray, hair oil, hair dye, mouth wash, some dentifrices and denture adhesives, bath salts, pine-scented oils and toilet preparations may cause reactions. Again, *the patient should use only prescribed cosmetics.*

Clothing, Bedding and Personal Contacts.—Troublesome reactions may occur from drip-dry and other finishes of cotton and other natural textiles. Although the formaldehyde treatment of cotton may be largely removed by washing, many cotton goods—especially bed linens—usually have a plasticized starch surface treatment which is capable of eliciting troublesome reactions and is not removed by laundering. Recently cleaned clothing, blankets or furs, or the pressing of recently cleaned materials may not be tolerated. DDT is used in some dry cleaning fluids, especially on

woolens. Direct contact with detergents or with bedding or clothing washed with detergents, or dried in gas dryers, or treated with disinfectants may cause reactions in susceptible persons. It often is necessary to avoid the use of rubber-containing garters, brassieres, girdles and corsets; electric blankets and other rubber-containing bedding and upholstery; such synthetic textiles as Nylon, Dacron, Orlon and others—especially when these come in direct contact with the skin as in undergarments, nightgowns, sweaters and robes. Although Rayon is the best tolerated synthetic textile and Nylon is next, their finishes may also cause reactions in the highly susceptible. Plastic brushes, combs, purses, powder boxes, plastic upholstered chairs, stools, tables and desks and plastic telephones may also cause symptoms as a result of direct contact. Formica rarely has been incriminated and only in the highly susceptible as a result of prolonged direct contact. Bakelite telephones and other bakelite plastics usually are tolerated.

Miscellaneous. — Contact with lubricating oils, liquid fuels, solvents, polishes, waxes, chemicals used in photography, bleaches or heavily chlorinated water in swimming pools may cause reactions. Numerous other chemical exposures have been incriminated, but their essential *occupational nature* precludes their detailed description here.

FOODS COMMONLY CONTAMINATED BY CHEMICALS

1. *Foods often containing spray residues:* (a) Apple, cherry, peach, apricot, nectarine, pear, plum, olive, currant, persimmon, strawberry, cranberry, raspberry, blueberry, boysenberry, pineapple, rhubarb, grape, orange, grapefruit and lemon. (b) Brussel sprouts, broccoli, cauliflower, cabbage, head lettuce, tomato (hot-house grown), celery, asparagus, spinach, beet greens, chard, mustard greens, endive, escarole, leaf lettuce, romaine, Chinese cabbage and artichoke. Most currently used sprays of the chlorinated hydrocarbon type are oil soluble and *permeate the food to which they are applied.* They are *not* removed by washing, peeling, soaking in water or vinegar, or by cooking. Root vegetables are apt to be free of spray residues unless contaminated in transit or in markets. (c) Lamb, beef, and sometimes pork and fowl may be contaminated by the animals having eaten sprayed forage and concentrating such oil soluble insecticides, herbicides or their vehicles in their *fats.* Chicken and turkey often contain residues of a synthetic hormone—stilbestrol.

2. *Foods often containing fumigant residues:* Dates, figs, shelled nuts, raisins, prunes and other dried fruits; wheat, corn, rye, barley, rice, dried peas, dried beans, lentils.

3. *Foods often containing bleaches:* White flour. Unbleached flour usually is available. Although white flour is often "enriched" with synthetic

chemicals, it is still *impoverished.* Freshly ground whole wheat flour is far more nutritious and better tasting.

4. *Foods often treated with sulfur:* Peach, apricot, and nectarine may be dusted with sulfur as a fungicidal agent. Commercially prepared fresh apple, fresh apricot, fresh peach and French fried potato may be treated with sulfur dioxide as an anti-browning agent. Molasses, dried fruit, melon and citrus candied peel and fruit marmalade may be bleached with sulfur dioxide. Dried apple, dried pear, dried peach, dried apricot, raisin, prune, corn syrup (glucose), corn sugar (dextrose), cornstarch and corn oil usually are treated with sulfur dioxide in the process of manufacture.

5. *Foods artificially colored:* Creme de Menthe, maraschino cherries and other colored fruit; Jello and other colored gelatin desserts; mint sauce, colored ice cream, colored sherbet, colored candy, colored cake, cookie and pie frostings and fillings; wieners, bologna, cheese, butter, oleomargarine; orange, sweet potato, Irish potato. Root beer, pop, cola drinks and certain other soft and imitation drinks usually contain coal-tar dyes.

6. *Foods artificially sweetened:* Any containing saccharine or Sucaryl (sodium cyclomate).

7. *Foods exposed to gas:* Bananas often are artificially ripened by exposure to ethylene gas. Apples and pears are sometimes stored in the presence of ethylene gas. Coffee is usually roasted over an open gas flame and may absorb some of the combustion products of such a flame. Cane and beet sugars usually are clarified by being filtered through bone char. These filters usually are reactivated periodically in gas-fired kilns. Absorbed combustion products apparently are imparted to the next batch of syrup which is filtered through them. Raw sugar may be somewhat less contaminated. Honey is the preferred sweetening agent.

8. *Foods contaminated by containers:* Carrot, parsnip, turnip, tomato and mixed shredded greens are sometimes dispensed in odorous plastic bags. Certain other foods may also be contaminated by having been transported, stored or frozen in plastic containers. Cellophane wrapped foodstuffs are usually tolerated by chemically susceptible patients. In general, plastic wrappings tend to contaminate their food contents in direct proportion to the odor emitted by the wrapping material. If odorous or if rubbing or filing the surface of a plastic wrapper causes the emission of an odor, there is increased reason for suspecting it. The longer a food remains in an odorous plastic wrapping, the more it may be contaminated. Plastic refrigerator dishes for storage of foods are commonly incriminated. Citrus fruit may be contaminated chemically by fungicide treated containers.

Foods are frequently contaminated by the golden brown lining of metal cans. This lining—most commonly a phenolic resin—prevents the metal from bleaching the can contents but also contaminates them chemically. Only such foods as the manufacturer desires to bleach (asparagus, grapefruit, pineapple, artichoke and some citrus juices) are apt to be packed in unlined tins.

9. *Foods often waxed with paraffin:* Rutabaga, parsnip, turnip, pepper, apple, orange, grapefruit, tangerine and lemon may be waxed and/or polished. Apple, cucumber, eggplant and green pepper may be lightly waxed and polished.

10. *Foods often containing desiccating agents:* Triscuits and prepared cocoanut often contain added glycols.

FOODS THAT USUALLY ARE LESS CHEMICALLY CONTAMINATED

Fish and *Meat:* Fresh or frozen seafood (lobster, crayfish or lobster tail, shrimp, crab and others), fresh fish or fish which has been frozen in large pieces (in contrast to pound packages) are not usually contaminated. Lean meat from which the fat has been stripped prior to cooking is preferable to cooking meat with its adherent fat.

Vegetables: Fresh potato (if undyed and home peeled), turnip, rutabaga, eggplant, and parsnip (if not waxed), tomato (if field ripened), carrot (if not bagged in odorous plastic), squash, onion, pumpkin, beet, (tops are usually sprayed), salsify, celery root, parsley root, okra, green peas and green beans (if fresh, fresh frozen or canned in glass).

Fruit: Nuts in shell only (Brazil nut, cocoanut, walnut, hickory nut, pecan, filbert, hazlenut).

Sweetening agents: Honey, sorghum and pure maple.

Fats and *Oils:* Olive, cottonseed, peanut, soy, cocoanut, sunflower, sesame, safflower, preferably *cold pressed* rather than extracted by the usual solvent processes. Buckwheat.

Importations such as chocolate, arrowroot, tapioca, carob and sassafras tea usually have been fumigated in shiphold.

Any food may have been contaminated in transit or in markets by sprayed surroundings in contaminated bulk cartons, plastic bags or DDT-treated burlap bags.

Uncontaminated Food Sources

Foods from approved local sources should be secured for canning in glass or freezing in glass or aluminum foil during the season of availability.

Membership in state and local National Food Associates groups or Organic Gardening Clubs is helpful in finding sources of supply.

DISCUSSION AND SUMMARY

Most persons remain adapted to the conditions of their existence without becoming specifically susceptible to various environmental substances and without manifesting ill health from exposure to them. Of those who do become susceptible to one or more environmental materials, including items of the diet, many remain specifically adapted for long periods without obvious ill effects. Sooner or later, however, adaptation tends to taper off and chronic symptoms ensue. Although this may involve a single excitant, susceptibility and maladaptation to multiple environmental exposures is the rule. Under such circumstances, the common causes of chronic ills are rarely suspected.

The range of manifestations encompass localized and constitutional reactions as well as physical and mental syndromes, including an alternating relationship between levels and phases of chronic and acute effects. The clinical picture presented at any given time depends principally on factors of specific exposure, susceptibility and adaptation in the sense of the body's over-all defenses.

The three major causes of reactions on the basis of individual susceptibility and exposure to environmental materials are: (1) inhaled particles (pollens, dusts, molds, danders, et cetera); (2) foods, and (3) chemical additives and contaminants of air, food, water, biological drugs and chemical drugs, as well as perfumes, cosmetics, and certain other man-made synthetic materials referred to as the *chemical environment.*

Individual susceptibility to the chemical environment or parts of it must be carefully differentiated from the *clinical effects resulting from other environmental excitants* with which it usually coexists. For instance, susceptibility to chemical additives and contaminants of the food supply must be separated from food susceptibility *per se.* Indeed, susceptibility to all three groups of environmental excitants is to be expected until *demonstrated not to exist.* Likewise, susceptibility to one or more potential excitants is not to be assumed until *demonstrated to exist.*

Because of the *unreliability of individual histories,* both of these tasks are facilitated by a program of comprehensive environmental control in which the most probable excitants are avoided concurrently. After chronic effects resulting from oft-repeated exposures have subsided, isolated re-exposures to which high degrees of susceptibility exist then induce acute reactions which demonstrate *cause and effect. Treatment consists of avoiding incriminated excitants,* thereby decreasing the load of materials to which adaptation is being attempted.

In contrast to naturally occurring relatively inert physical and biological substances capable of inducing specific susceptibility and manifesting as chronic illness, the *man-made chemical environment* is both more recent and more reactive.

Although many seem to be adapting satisfactorily to these new living

conditions, susceptibility to one or more facets of the chemical environment apparently is increasing as the totality of such exposures accumulate. It would appear only a matter of time before many of those apparently adapting satisfactorily to one or more of these exposures succumb to the oft-repeated thrusts of a given facet of the chemical environment. Once such a maladaptation has occurred, susceptibility not only tends to *increase in degree* but appears to *spread* to related materials to which frequent exposures also occur. Chronic illness ensues as adaptive abilities wear down. Whereas at first these changes occurred principally in the elderly and the young, they are now becoming increasingly common in middle age as well as during reproductive and adolescent years.

Despite the rapidly increasing knowledge of the chemical makeup of the world and the ability of the human race to construct a *chemical environment, man remains a biologic phenomenon.* Individual man adapts or fails to adapt to the circumstances of his existence, as does any other living thing. Despite our rapidly increasing knowledge of the chemical basis of physiology, we are unable, as yet, to avoid the development of such maladapted states associated with chronic symptom syndromes or to reverse the course of this process, once it has developed.

One cannot escape the deduction that susceptibility to and maladaptation to the chemical environment and illnesses associated therewith are early manifestations of degeneration. Whatever it may be called, one thing is certain: individuals who become highly susceptible and maladapted to one or more common chemical excitants are usually *not the same thereafter.* Although many may be maintained symptom-free in a controlled or more primitive existence, such avoidance programs are becoming increasingly difficult to maintain, due to the increasing ubiquity of chemical surroundings. Moreover, a symptom-free state may also be precluded by the common coexistence of individual susceptibility to various physical and biological exposures which are also impossible to avoid.

However, the general rule that *finding and avoiding causes of illness is better than treating the effects of illness* still holds. Despite the restrictive nature of the therapeutic program, the outlook for the chemically susceptible person is far less bleak than may be inferred from the above generalizations. First of all no person is susceptible to all the facets of the chemical environment. Many times the relatively few chemical excitants impinging on a patient may be easily avoided. Secondly, if the degree of susceptibility is not excessive, avoidance of massive doses may be sufficient to relieve symptoms. Such a person may then be able to adapt satisfactorily to lesser doses which cannot be avoided as readily. Lastly, it is a great source of satisfaction to a chronically ill person to know *why* he is sick—even though a completely satisfactory solution to his problem may not be available as a result of avoiding incriminated causes. At least, having a specific diagnosis and attempting to avoid incriminated excitants tends to break the everlasting continuity of undiagnosed chronic illness resulting

from daily exposures. Although acute reactions arising from *accidental exposures* may be temporarily more severe than the previous level of chronic symptoms, such acute responses are ordinarily of relatively short duration and may be treated much more effectively. Moreover, acute reactions of *known causation* are infinitely more endurable than chronic illness of *unknown origin.*

The more commonly pursued alternative of treating the effects of chronic illness without demonstrating its causes may be especially hazardous for the chemically susceptible person. When already susceptible and reacting to one or more chemical excitants, the use of *additional* synthetically derived chemical drugs is neither sound nor effective. Under such circumstances, superimposed acute or chronic reactions are to be expected, in view of the ease with which susceptibility tends to spread to materials of common genesis. All too frequently, such a course adds to the victim's total burden by complicating or perpetuating his illness.

This presentation purposely has emphasized the *totality of the chemical environment* to which the most highly susceptible person may react, for two reasons:

1. This is an effective teaching method, for once the total scope and extreme manifestations of a clinical problem are grasped, more commonly occurring but lesser degrees of the same problem tend to be more apparent.
2. This is more practical as compared with the way this subject has ordinarily been presented. This orientation, stressing *multiple reactions of a single person,* is more helpful to the practitioner sitting across from a sick patient than a knowledge of the *statistical incidence of reactions* to certain chemical compounds occurring in a *large group of subjects.*

In summary, this presentation deals with MAN as a *biological unit* and his *adaptation to a chemically contaminated world.*

REFERENCES

44. Clark, H. G. and Randolph, T. G.: The acid-anoxia-endocrine theory of allergy. J. Lab. & Clin. Med., 36:811-812, 1950.
45. Randolph, T. G. and Clark, H. G.: Sodium bicarbonate in the treatment of allergic conditions. J. Lab. & Clin. Med., 44:915, 1954.
46. Godlowski, Z. Z.: Endocrine management of selected cases of allergy based on enzymatic mechanism of sensitization. A.M.A. Arch. Otolaryng., 7:515-557, 1960.
47. Randolph, T. G. and Clark, H. G.: Discussion of observations on the metabolic changes resulting from the administration of ACTH to patients with asthma and allied conditions. *In* Rose, B.; Pare, J. A. P.; Pump, K. K.; Sanford, R. L.; Mackenzie, K. R. and Venning, E. H.: Proc. of the Second Clinical ACTH Conference, Vol. 1—Research, p.p. 525-527. New York: Blakiston, 1951.
48. Singer, R. B., Clark, J. K., Barker, E. S., Crosley, A. P., Jr., and Elkingon, J. R.: The acute effects in man of rapid intravenous infusion of hypertonic sodium bicarbonate solution. Medicine, 34:51-95, 1955.
49. Randolph, T. G. and Rollins, J. P.: Adrenocorticotropic hormone (ACTH); its effect in atopic dermatitis. Ann. Allergy, 9:1-10, 1951.

The Shape of Things to Come

Mechanism of increase of endotoxin susceptibility in animals showing delayed hypersensitivity.
J. Johanovský, M. Vrána, O. Vejbora and D. Francová, Nature 190:182 (Apr 8) 1961.

The mechanism of acetylcholine effect on the pulmonary circulation. (In Russian, abstract in English)
A. I. Khomazyuk and A. A. Moibenko, Bull Exp Med Biol (USSR) 51:3 (Feb) 1961

Diagnostic significance of some immune reactions in rheumatism. (In Russian)
I. M. Lyampert et al., J Microbiol Epidermiol Immunol (USSR) 3:28, 1961

Unusual electrophoretic patterns of plasma proteins in human subjects.
E. L. Kanabrocki, Clin Chem 7:107 (Apr) 1961

Metabolic incorporation of L-[^{14}C] valine into protein and bound non-protein forms in Italian ryegrass.
R. L. M. Synge and M. A. Youngson, Biochem J 78:708 (Apr) 1961

Metabolic fate of a synthetic corticosteroid (triamcinolone) in the dog.
J. R. Florini, L. L. Smith and D. A. Buyske, J Biol Chem 236:1038 (Apr) 1961

Reactivation of rabies virus infection with adrenocorticotropic hormones.
O. A. Soave, H. N. Johnson and K. Nukamura, Science 133:1360 (Apr 28) 1961

Release of 5-hydroxytryptamine from rat mast cells in vitro.
G. T. Archer, Nature 190:350 (Apr 22) 1961

Production of pyrogenic substances by extracts of delayed hypersensitive cells mixed with antigen in vitro.
J. Johanovský, Nature 190:355 (Apr 22) 1961

Effects of irradiation of chest on pulmonary function in man.
C. Emirgil and H. O. Heinemann, J Appl Physiol 16:331 (Mar) 1961

The significance of the regional lymphatic system in the genesis of transplantation immunity.
J. Vrubel, Folia Biol 7:103 (Feb) 1961

The question of the choice of method to induce antitumour isoimmunity and isoimmunity within a group of mice with controlled antigenic homogeneity.
P. Koldovský, Folia Biol 7:115 (Feb) 1961

Species-specific antigens in human tissue cultures.
T. Vainio, Acta Path Microbiol Scand Suppl 144, 51:185, 1961

Effects on amine oxidase of substances which antagonize 5-hydroxytryptamine more than tryptamine on the rat fundus strip.
R. B. Barlow, Brit J Pharmacol 16:153 (Apr) 1961

Some inhibitors of histamine-induced and formaldehyde-induced inflammation in mice.
B. J. Northover and G. Subramanian, Brit J Pharmacol 16:163 (Apr) 1961

Metabolism of [^{14}C]-Histamine in heart-lung-liver preparations of cats.
B. Lilja and S.-E. Lindell, Brit J Pharmacol 16:203 (Apr) 1961

The production of "delayed type" cutaneous hypersensitvity to human donor leukocytes as a result of the rejection of skin homografts.
J. P. Merrill, E. A. Friedman, R. E. Wilson and D. C. Marshall, J. Clin Invest 40:631 (Apr) 1961

Pulmonary function studies used to evaluate air pollution asthma disability.
H. W. Phelps, Milit Med 126:282 (Apr) 1961

New methods for the study of percutaneous absorption.
K. Wilson, Drug Cosm Ind 88:444 (Apr) 1961

The release of histamine from rabbit platelets by means of anitgen-antibody precipitates. II The role of plasma in the release of histamine.
J. F. Barbaro, J Immunol 86:377 (Apr) 1961

Papers of Interest

Berry, D. G., et al.: Exacerbations of chronic bronchitis treatment with oxytetracycline. Lancet, 1:137 (Jan. 16) 1960.

A population of fifty-eight patients afflicted with chronic bronchitis was subjected to double-blind controlled studies. Those of the patients who were moderately severely affected recovered sooner or showed less pulmonary deterioration than did the controls or those only mildly affected by their infectious disorder.

Barefoot, S. W.: Cutaneous reactions encountered in four-hundred patients treated with sulfamethoxypyridazine. N. Carolina Med. J., 20:471 (Nov.) 1959.

Sulfamethoxypyridazine (Midicil) is reported as controlling pustular and cystic lesions in acne as well as any antibiotic used. The reaction rate was less than 3 per cent.

Paz, F. and Christian, J. R.: A safe theophylline preparation for pediatric use. Clin. Med., 6;2311 (Dec.) 1959.

Dyspnea relieved in thirty minutes in eight patients. Twenty-two others were noticeably improved over a period of two to five days.

Gardner, P. S., McGregor, C. B. and Dick, K.: Association between diarrhoea and adenovirus type 7. Brit. Med. J., 1:91 (Jan. 9) 1960.

Adenovirus type 7 was isolated from the stools of ten patients afflicted with diarrhoea and vomiting. In some, symptoms referred to the respiratory tract were also present.

Kahlson, G.: A place for histamine in normal physiology. Lancet, 1:67 (Jan. 9) 1960.

Suggests histamine as a physiological substance which is not derived from mast cells and is related to metabolic processes associated with growth and repair.

Gurvich, A. E., Kapner, R. B., and Nezlin, R. S.: Isolation and examination of pure antibodies, prepared by the use of antigens fixed on cellulose. Biochemistry (USSR), 24:129 (Jan.-Feb.) 1959.

When antigens are fixed on cellulose, quantitative removal from immune sera is possible. Other antibodies are not affected.

Liebowitz, D. and Ritter, H., Jr.: Anaphylactic reaction to chymotrypsin. J.A.M.A., 172:159 (Jan. 9) 1960.

In a forty-four-year-old patient in whom no history of allergy was apparent, intramuscular injection of chymotrypsin was followed by an anaphylactic type of reaction which responded to epinephrine and corticosteroid hormones.

Johnston, D. H., Cornish, A. L.: Acute pancreatitis in patients receiving chlorothiazide. J.A.M.A., 170:2054 (Aug. 22) 1959.

Following daily doses of 0.5 to 1.0 grams of chlorothiazide for two to three months, acute pancreatitis, possibly due to the drug, developed in three female patients.

Cohen, T.: Hypokalemic muscle paralysis associated with administration of chlorothiazide. J.A.M.A., 170:2083 (Aug. 22) 1959.

Hypokalemia subsequent to the use of the drug presented itself as muscular weakness and paralysis as noted in the left thigh and the right arm. No other muscle groups were affected.

Floch, M. and Leibowitz, S.: Hemorrhage from multiple sites associated with Chlorpromazine-induced jaundice. J.A.M.A., 170:2060 (Aug. 22) 1959.

Treatment with vitamin K reversed hypoprothrombinemia, toxicity and hemorrhage in a sixty-six-year-old female patient who had for seventeen days taken 7.5 mg daily.

Granier, L. W.: Exfoliative dermatitis as a complication of chloroquine (aralen) therapy in rheumatoid arthritis. A.M.A. Arch. Dermat., 77:722 (June) 1958.

The onset of the signs and symptoms occurred twenty days following the initiation of treatment with a single dose of 250 mg chloroquine daily, in a patient in whom there was no previous history of either dermatitis or allergy or any type of drug sensitivity.

Welsh, Ashton L. and Ede, Mitchell: Generalized eruption with triacetyloleandomycin. AM&CT, 7:173 (Mar.) 1960.

A case report of severe generalized cutaneous manifestation of reaction to triacetyloleandomycin is given.

Hudson, A. L.: A new drug for control of itching—trimeprazine (1°-(3-dimethylamino-2 methylpropyl)-phenothiazine). J. Canadian Med. Assn., 80:125 (Jan. 15) 1959.

Of thirty patients with atopic eczema and generalized neurodermatitis, all were relieved of pruritis when 5 mg before each meal and 10 mg before bedtime was given. Some had only moderate relief, but a few had complete freedom, especially from nocturnal pruritis.

Dowling, H. F., Mellody, M., Lepper, M. H. and Jackson, G. G.: Bacteriologic studies of the sputum in patients with chronic bronchitis and bronchiectasis. Results of continuous therapy with tetracycline, penicillin, or an oleandomycin-penicillin mixture. Am. Rev. Respiratory Dis., 81:329 (Mar.) 1960.

The antibiotic agents administered reduced the number of staphylococci, pneumococci and of H. influenzae.

Banyai, Andrew L.: Mechanism of cough and its control. GP, 21:83 (Mar.) 1960.

Comprehensive review of complex problem by internationally famous expert.

Reinhold, M.: Relationship of stress to the development of symptoms in alopecia areata and chronic urticaria. Brit. Med. J., 1:846 (Mar. 19) 1960.

Stress reported to be etiological factor in some of fifty-two patients affected with alopecia areata and twenty-seven others with urticaria.

Knudtson, K. P.: The pathologic effects of smoking tobacco on the trachea and bronchial mucosa. Am. J. Clin. Pathol., 33:310 (Apr.) 1960.

A known history of smoking, patient age and geographical location were correlated with changes in the lungs. One hundred and fifty patients were studied post-mortem. The tissue was normal in only 20 per cent of the heavy smokers. The mucous membrane was normal in 50 per cent of those who did not smoke.

Beall, G. N., and Vanarsdel, P. P., Jr.: Histamine metabolism in human disease. J. Clin. Invest., 39:676 (Apr.) 1960.

Radioactive histamine is cleared from the blood and excreted by means of the kidney in thirty hours. It appears that histamine is rapidly activated, degraded and excreted. By means of such quantitative techniques, no abnormality in the metabolism of histamine was found to be present in patients with adrenal or hepatic insufficient function, and no abnormality was present in those patients known to be affected with histaminic cephalalgia or bronchial asthma.

Brunner, M. J. and Finkelstein, P.: A laboratory method for evaluation of topical anti-inflammatory agents. Arch. Dermatol., 81:453 (Mar.) 1960.

When the epidermis is irritated by means of a patch test of tetrahydrofurfuryl alcohol, the anti-inflammatory effects of corticosteroid hormones can be measured. Fourteen hormones were studied and hydrocortisone, in a concentration as low as 0.1 per cent, proved to be anti-inflammatory.

Beck, C., Levine, A. J., Davis, O. F. and Horwitz, B.: Clinical studies with an oral anti-inflammatory enzyme preparation.

The anti-inflammatory effects of oral chymotrypsin preparations were said to parallel those given parenterally as noted in a study of 106 patients in whom improvement occurred in approximately 75 per cent.

Townsend, E. H., Jr.: Chemoprophylaxis during respiratory infections in a private pediatric practice. J. Dis. Children, 99:566 (May) 1960.

Of 845 infants and children whose ages ranged from two months to twelve

years, 303 received treatment for symptoms only, 309 were given antimicrobial agents while 233 received prophylactic doses of antibacterial drugs. The respective percentages of complications were 8.9, 14, and 8.4 per cent.

Disturbing conclusion.

Beasley, A. R., Sigel, M. M., Schlaepfer, G. G., Edwards, H. K., Mangels, M. and Wellins, F. M.: Antibody responses of children to asian influenza vaccine. J. Florida Med. Assoc., 46:1367 (May) 1960.

Results show that even 20 CCA units administered intradermally in children and in young and middle-aged adults will evoke an antibody response. The injection must be repeated, for better protection follows the use of larger amounts.

Carryer, H. M., Sherrick, D. W. and Gastineau, C. F.: Occurrence of allergic disease in patients with adrenal cortical hypofunction. J.A.M.A., 172:1356 (March 26) 1960.

Of 496 patients suffering from hypofunction of adrenal cortical tissue, 45 had allergic disorders. Appraisal of the influence of replacement treatment was made in eight patients in all of whom, improvement of the allergic disorder was noted.

Rhodes, A. J.: Recent advances in virus infections: the new era in virology. Brit. M. J., 1:1071 (Apr. 9) 1960.

Viruses, of which more than 150 have been studied, are responsible for more disorders than are caused by bacteria.

Wahner, H. W. and Peters, G. A.: An evaluation of some newer antihistaminic drugs against pollinosis. Proc. Staff Mtgs. Mayo Clin., 35:161 (Mar. 30) 1960.

For relief of symptoms, 10-(1-methyl-3-pyrrolydylmethyl) phenothiazine HCL and chlor-trimeton head the list. Following was N-benzhydryl-N'-cinnamyl-piperazine. Isothipendyl HCL was responsible for more drowsiness, headache and chemical taste, and in this group, was the least effective agent tested.

Winkelmann, R. K.: Diagnosis and treatment of allergic angiitis (anaphylactoid purpura). Postgrad. Med., 27:437 (Apr.) 1960.

Allergic angiitis is acute. Treatment consists of bed rest, transfusions, elimination of any chemical, drug or food known to cause or aggravate the disorder, coupled with the use of antihistaminic agents and often corticosteroid hormones.

Wilson, J. S., Grant, P. J., Miller, D. L., Taylor, C. E. D. and McDonald, J. C.: Trial of adenovirus vaccine in royal air force recruits. Brit. M. J., 1:1081 (Apr. 9) 1960.

In four hundred and two recruits, each treated with one subcutaneous injection of 1 ml of a polyvalent vaccine consisting of adenoviruses types 3, 4 and 7, reduction of the 40 per cent admission rate for respiratory illness was noted more than one week from inoculation. Protection is approximately 70 per cent.

Rothenberg, P. A. and Hall, C.: Agranulocytosis following use of imipramine hydrochloride (tofranil). Am. J. Psychiat., 116:847 (Mar.) 1960.

First case report.

Boger, W. P., Aaronson, H. G. and Frankel, J. W.: Asian influenza. Persistence of antibodies and revaccination. New England J. Med., 262:856 (Apr. 28) 1960.

In 2432 patients treated with 1 ml of a polyvalent influenza vaccine consisting of 500 CCA units of Asian virus, no local or systemic reactions were noted. The hemagglutination-inhibiting antibodies increased more than five multiples and in 87 per cent of the patients, high titers were observed twelve months following the injection.

Gregg, J. A. and Maycock, R. L.: Thrombocytopenia induced by administration of sodium para-aminosalicylate. J.A.M.A., 172:1902 (Apr. 23) 1960.

A sixty-three-year-old male patient responded to administration of sodium p-aminosalicylate and streptomycin with thrombocytopenic purpura and massive gastrointestinal hemorrhage. The readministration of the p-aminosalicylate was followed by recurrence of the thrombocytopenia.

Josephson, A. S.: The development of antibodies to penicillin in rabbits. J. Exper. Med., 111:611 (May 1) 1960.

In rabbits, administration of penicillin caused the appearance of antibodies not related to the antimicrobial activity of the antibiotic agent.

News Items

AMERICAN COLLEGE OF ALLERGISTS

There are available thirty copies of the abstract books of the Graduate Instruction Course of the American College of Allergists held in Dallas in March. These may be obtained by sending $1.00 to Dr. John Gillaspie, 2141 14th Street, Boulder, Colorado.

FLORIDA ALLERGY SOCIETY

At a recent meeting of the Florida Allergy Society, the following officers were elected:

President.....Solomon D. Klotz
President-Elect.....Benjamin A. Johnson
Secretary-Treasurer.....Jack A. Rudolph

GRADUATE COURSE IN MEDICAL HYPNOSIS

Under the auspices of the University of Pennsylvania Graduate School of Medicine, a graduate course in Medical Hypnosis is being offered to physicians and dentists. There will be twenty-four weekly afternoon sessions, beginning October 4. The course will be given at the Institute of the Pennsylvania Hospital, Philadelphia, Pennsylvania.

CANADIAN ACADEMY OF ALLERGY

At the annual meeting of the Canadian Academy of Allergy, the following officers were elected:

President.....Dr. J. H. Toogood
Vice President.....Dr. C. Collins-Williams
Secretary-Treasurer.....Dr. H. L. Bacal

POSTGRADUATE COURSE IN IMMUNOLOGY, HYPERSENSITIVITY AND PULMONARY FUNCTION

Because of the meeting of the Fourth International Association of Allergology in New York City in October, the annual Postgraduate Course in Immunology, Hypersensitivity and Pulmonary Function of the Children's Hospital in Washington, D. C., has been postponed until November 17, 18 and 19, 1961.

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Book Reviews

MANUAL OF CUTANEOUS MEDICINE. By Donald M. Pillsbury, M.D., Walter B. Shelley, M.D. and Albert M. Kligman, M.D., Philadelphia and London: W. B. Saunders Company, 1961, 430 pages. Price: $9.50.

This book is not a condensation of the monumental text, *Dermatology,* written by the same authors in 1956, but rather an entirely new text with different words and, for the most part, different illustrations. It is approximately one-third the length and even more terse than their preceding text. Like the preceding text, it eliminates many of the errors and shibboleths perpetuated with the permanence of flies in amber in succeeding editions of other texts. All three authors are professors at the University of Pennsylvania. All have had almost unparalleled experience both in clinical dermatology, and in research dermatology.

If this text has a fault, it would be that is it ultra-conservative in its recommendations for treatment. It is extremely forthright in its opinion of many skin diseases and states that either no treatment is of any effect or that the merits of a treatment are not improved. It does not make the assumption that tacit acceptance of bad treatment is better than none. Ancient theories of etiology and of treatment based upon unproved hypotheses, supposition or incrustation of legend from the past are rigidly eschewed.

This book will be useful to practitioners, or students who do not wish to spend the money or have the detail available in the larger text by the same authors. It is written in the same interesting, and lively style as the previous text. In an era when it is almost obligatory for medical writing to be jejune, this text reads as easily as an article in a popular as contrasted to a medical journal.—MCZ

HOW TO MASTER YOUR ALLERGY. By Harry Swartz, M.D., F.A.C.A. New York: Thomas Nelson & Sons, 1961, 219 pages, 12 appendices. Price: $5.00.

This book, written expressly for the lay reader, is explicit, and each subject is well amplified. The last five pages summarize, for the physician, all that has been stated in the previous 214 pages as written for the layman.

The style is lucid; the vocabulary is expressive, and the presentation of the clinical material is uncomplicated. Without losing sight of the technical accuracy of the material, moreover, the author has written an elemental text. Especially illuminating and absorbing are the case histories of which there are many.

The author has consistently kept his lay audience in mind. He is never scientifically abstract nor medically prolix. The format of each chapter is enhanced by an ample number of subdivisions, and the salient points are summarized. The book is eminently readable because of the type of print which is large and well-spaced. The chapter headings themselves are printed in bold face.

An enlightening and comprehensive explanation of what allergy is and what it does is presented in the first chapter. The author's statistics concerning the number of allergic sufferers quietly reinforce the verity of his text.

The second chapter, entitled, "Emotions and Allergy: A Two-Way Street", illuminates an aspect of allergy which is, for the most part, least understood by the allergic patient. The author does not attempt to give the reader a course in abnormal psychology nor does he encourage lay psychoanalysis. The evident purpose of this chapter is to make the allergic patient aware of some of the psychological implications of his allergic disorder. The author stresses the somatopsychic

aspects of allergy and states that undue emphasis is placed on the psychosomatic types of disturbances.

There are detailed discussions of what precautions should be taken during a patient's infancy, childhood, and in the case of female patients, pregnancy. In sequence are chapters concerned with the diverse phases of allergic disorders of adult life. To choose three of several chapters, all equally pertinent, those entitled, "Building a House", "Going to the Hospital" and "Female Hormones and Allergy" are exemplary of the author's exhaustive compilation.

Twelve appendices include lists such as the trees which cause hay fever, mechanical and electronic aids, and hypoallergenic cosmetics.

The author has written an easily comprehensible, logical and, for the most part, realistic and prophylactic program for the allergic or potential allergic patient who, like others, needs written instructions to supplement those given orally.

The publication of this excellent small volume should be a boon to those affected by allergic reactions.

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Center Laboratories ..... Port Washington, New York
Complete Allergy Service "from Solution to Syringe"

Dalare Associates ..... Philadelphia, Pennsylvania
Propeptans for Food Allergy

The DeVilbiss Company ..... Somerset, Pennsylvania
Atomizers and Nebulizers

Hollister-Stier Laboratories ..... Spokane, Washington; Yeadon, Pennsylvania; Chicago, Illinois; Atlanta, Georgia; Los Angeles, California; Oakland, California
The Home of Personalized Allergy Service

Knoll Pharmaceutical Company ..... Orange, New Jersey
Makers of Quadrinal

Luzier's, Inc. ..... Kansas City, Missouri
Makers of Fine Cosmetics and Perfumes

Ralston-Purina Company ..... St. Louis, Missouri
Ry-Krisp

Rexair Incorporated ..... Detroit, Michigan
Producers of the Rainbow Conditioner and Cleaner

Schieffelin & Co., Almay Division ..... New York, New York
Manufacturers of Hypoallergenic Cosmetics

Texas Pharmacal Company ..... San Antonio, Texas
Manufacturers of Allercreme Hypo-Allergenic Products

Warner-Chilcott Laboratories ..... New York, New York
Makers of Tedral